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STERNAL PUNCTURE.[1]

By JOHN A. MCLEAN, M.D., M.R.C.P., M.R.A.C.P.,

Honorary Physician to Out-Patients, Alfred Hospital, Melbourne. From the Baker Medical Research Institute, Melbourne.

STERNAL puncture is a simple procedure for the examination of bone marrow cells during life, and since its introduction by Arinkin in 1929 it has been used by hæmatologists as a supplementary means of investigating obscure blood diseases. There has been some controversy as to the relative values of sternal puncture and sternal biopsy, as recently described by Wilson.[(1)] More information is available from sections and smears than from smears alone; but the greater technical difficulties and the necessity for carefully prepared histological sections are a disadvantage compared with the simplicity of a method that gives adequate information for clinical diagnosis.

During the last two years I have performed 120 sternal punctures on patients attending the out-patient department or in the wards of the Alfred Hospital, and the purpose of this paper is to present the results of this investigation and to assess the value of the method in routine hæmatology.

Technique.

The technique employed is as follows:

A lumbar puncture needle, with an external diameter of 1·6 millimetres, was cut down to 2·5 centimetres and fitted with an adjustable stop to control the depth of puncture. The female joint of the needle was enlarged to take a "Vim" syringe of a capacity of one cubic centimetre. Prior to use the needle and syringe were autoclaved in a glass test tube plugged with cotton wool. After a preliminary injection of a 2% solution of "Novocain" in the skin and subperiosteum the sternum was punctured just outside the mid-line at the level of the third costal cartilage. Approximately 0·1 cubic centimetre of marrow fluid was aspirated and film preparations were made on glass slides. The films were stained by the Jenner-Giemsa method and were examined under the low power of the microscope and with the oil immersion lens.

Terminology.

There is confusion in the terminology of primitive red blood cells. The terms megaloblast, erythroblast and normoblast are applied with different meanings by different hæmatologists, and it is therefore necessary to state the criteria by which these cells are classified. The megaloblast is defined as a nucleated red cell in which the nuclear chromatin appears as a fine network with several neucleoli and in which the cytoplasm may be basophilic, polychromatophilic or eosinophilic, according to the content of hæmoglobin and the method of staining. The characteristic feature is the structure of the nucleus, and this distinguishes the cell from the erythroblast, in which the nuclear chromatin is in coarse strands and aggregations, and from the normoblast, in which the nucleus is pyknotic (Figure I). The megaloblast is a larger cell than are the erythroblast and normoblast; but occasionally macroerythroblasts and macronormoblasts are seen, and one cannot differentiate these cells on the basis of size. Some hæmatologists regard that type of megaloblast with eosinophilic cytoplasm as a cell in which the rate of maturation of the cytoplasm exceeds that of the nucleus. There is a tendency to subdivide nucleated red cells into many groups. Thus Scott[(2)] describes ten; but to extend the differential count in bone marrow films in such a way makes the procedure unnecessarily com-

[1] Work done with the aid of a grant from the National Health and Medical Research Council.

TABLE I.

Case Number.	Sex of Patient.	Age. (Years.)	Results of Differential Cell Count. (Percentages.)														Leuco-erythrogenetic Ratio.
			Myeloblasts.	Premyelocytes.	Myelocytes.	Young Meta-myelocytes.	Band Meta-myelocytes.	Neutrophiles.	Eosinophiles.	Basophiles.	Lymphocytes.	Monocytes.	Megaloblasts.	Erythroblasts.	Normoblasts.	Plasma Cells.	Turk Cells.	
I	M.	65	2·0	2·4	13·2	8·8	14·8	16·0	0·8	0·0	5·6	0·0	0·0	17·2	18·0	1·2	—	0·8
II	M.	28	1·6	0·8	12·0	9·6	18·8	20·0	2·8	0·0	15·2	1·2	0·0	8·4	8·0	0·8	0·8	1·4
III	M.	31	1·0	0·5	6·5	5·5	12·0	33·0	1·0	0·0	21·5	2·5	0·0	11·5	5·0	—	—	0·8
IV	M.	24	1·6	0·8	14·8	8·4	15·6	15·6	1·2	0·0	9·2	0·8	0·4	15·2	14·8	0·8	0·8	0·8
V	M.	29	1·2	0·8	18·8	11·2	12·4	17·2	1·2	0·4	17·2	0·4	0·0	2·8	14·8	1·2	0·0	1·7
VI	M.	33	1·0	5·0	13·0	3·0	19·0	12·0	0·0	0·0	18·0	8·0	0·0	10·0	5·0	—	7·0	2·7
VII	F.	50	2·0	0·8	8·8	6·0	12·0	16·4	0·8	0·4	17·2	0·8	0·8	17·6	15·6	0·4	0·4	0·5
VIII	F.	49	1·6	6·4	14·4	10·8	16·0	13·2	1·6	0·0	4·8	0·0	0·8	20·4	9·2	0·8	—	1·0
IX	F.	65	4·5	2·0	11·0	10·5	13·5	24·5	2·0	0·0	18·5	2·5	1·0	6·0	4·0	—	—	2·5
X	F.	40	0·8	1·6	9·6	6·4	6·8	32·4	0·4	0·4	22·4	1·6	0·0	8·8	8·8	—	—	1·1
XI	F.	60	3·2	5·2	6·8	9·6	22·4	22·0	1·2	0·4	8·4	0·0	1·2	9·6	8·4	1·2	0·4	2·4
XII	F.	65	2·0	4·5	10·5	9·5	17·0	14·5	2·5	0·5	2·5	0·5	1·0	20·0	12·5	1·0	0·5	1·8
																	Average	1·4

plicated and gives no practical advantages over the simple classification into three cell types as described above.

The primitive white blood cells found in the bone marrow have been classified into myeloblasts, premyelocytes, myelocytes, young metamyelocytes, band metamyelocytes, and neutrophile, eosinophile and basophile cells. Other cells included in the differential count are lymphocytes, monocytes, plasma cells and Turk cells.

Results of the Differential Count in Normal Persons.

As is shown in Table I, in which are tabulated the results from twelve normal persons taken at random from an out-patient clinic, there are considerable variations in the results of the differential count in normal subjects. A comparison with normal values obtained by other workers in much larger series of cases is shown in Table II. The results in the three series correspond fairly well and afford a basis upon which can be assessed the extent of normal variation.

TABLE II.

Bone Marrow Cell.	Mean Values in Percentages. Segerdahl.[3] (110 Cases.)	Maximum and Minimum Values in Percentages.	
		Hynes.[4] (41 Cases.)	McLean. (12 Cases.)
Myeloblast	1·32	0·0 to 2·5	1·0 to 4·5
Premyelocyte	1·35	0·0 to 5·0	0·5 to 6·4
Myelocyte	16·37	2·0 to 8·0	6·5 to 18·8
Young metamyelocyte	15·69	2·5 to 12·0	3·0 to 11·2
Band metamyelocyte	10·48	20·0 to 40·0	6·8 to 22·4
Neutrophile cell	20·86	9·0 to 30·0	13·2 to 33·0
Eosinophile cell	1·44	0·0 to 3·0	0·0 to 2·8
Basophile cell	0·14	0·0 to 0·5	0·0 to 0·5
Lymphocyte	16·76	5·0 to 20·0	2·5 to 22·4
Monocyte	2·27	0·0 to 5·0	0·0 to 8·0
Megaloblast	12·88	0·0 to 4·0	0·0 to 1·2
Erythroblast		2·0 to 7·0	2·8 to 20·4
Normoblast		7·0 to 19·0	4·0 to 18·0
Plasma and Turk cell	0·39	0·0 to 1·0	0·0 to 1·6

In the simplest terms the relative activities of leucopoiesis and erythropoiesis can be expressed as the ratio of total white cells to total nucleated red cells. The average normal value for this ratio is given as 6 (Zanaty[5]). As immature and mature white cells are included in this ratio against immature red cells, it has been suggested (Pontoni[6]) that a more accurate indication of the relation between leucopoietic and erythropoietic activities would be given if mature white cells were omitted. Such a ratio between immature cells of granulocyte series, from myeloblast to young metamyelocyte, and total nucleated red cells is known as the leucoerythrogenetic ratio. The mean value for this ratio in the series of results from normal persons set out in Table II is 1·4.

When the investigation was commenced cell counts were made on the aspirated fluid; but aggregations of adherent cells were frequently present, and it was manifestly impossible to make a satisfactory cell count. Examination under low power magnification of films from twelve normal persons established an approximate normal value for cellularity. The cellularity of films from abnormal persons was accordingly expressed as increased, normal or diminished (Figures IIA, IIB, IIC).

The Differential Count in Various Blood Diseases.

Macrocytic Anæmia.

Sternal puncture is of value in differentiating pernicious anæmia from other types of macrocytic anæmia. The 34 cases of macrocytic anæmia shown in Table III were originally diagnosed as of pernicious anæmia; but examination of bone marrow cells revealed that only ten cases were of the pernicious anæmia type, and this finding was confirmed by response to liver therapy.

Pernicious anæmia in relapse is characterized by a great increase in megaloblasts in the bone marrow (Peabody[7]), and this feature is readily observed in bone marrow smears. The mean value for megaloblasts in differential counts in the ten cases shown in Table III is 27·9%; this indicates a predominance of megaloblasts in the bone marrow.

There was a greater increase in cellularity of the films in pernicious anæmia than in the other types of macrocytic anæmia; but this finding was not of diagnostic significance.

As remission occurs in pernicious anæmia there is a change in the cytology of the bone marrow towards normal, and in two cases repeated sternal punctures revealed a great reduction in the number of megaloblasts as improvement occurred after treatment by liver extract. Even in remission there is an increase in the number of megaloblasts above the normal value as given in Table I. If there is no increase in the number of megaloblasts one can assert that the patient is not suffering from pernicious anæmia; but if there is an excessive number of megaloblasts, it does not follow that the disorder is necessarily pernicious anæmia. In 19 cases of macrocytic anæmia, proved to be not pernicious anæmia, the number of megaloblasts was, with the exception of two cases, not significantly increased. In these two cases there was an increase of 27·0% and 29·5% respectively in the number of megaloblasts, and there were several unusual features which make them worthy of record. The clinical histories are briefly as follows:

CASE XXVIII.—A female patient, aged fifty-one years, complained of weakness, loss of weight and occasional vomiting attacks of sixteen months' duration. Six months previously she had had ulcers on the tongue. On examination a pale emaciated appearance was observed. The tongue was moist and red and the papillæ were atrophied. No

TABLE III.

Case Number.	Sex of Patient.	Age. (Yrs.)	Hæmoglobin Value (Grammes) per 100 Cubic Centimetres.)	Red Cells in Millions per Cubic Millimetre.	Mean Corpuscular Volume in Cubic Microns.	Bone Marrow Cellularity.	Results of Differential Count of Bone Marrow. (Percentages.)														Leucoerythrogenetic Ratio.	Diagnosis.
							Myeloblasts.	Premyelocytes.	Myelocytes.	Young Metamyelocytes.	Band Metamyelocytes.	Neutrophiles.	Eosinophiles.	Basophiles.	Lymphocytes.	Monocytes.	Megaloblasts.	Erythroblasts.	Normoblasts.	Plasma Cells.	Turk Cells.		
XIII	M.	75	7·9	2·2	130	Increased.	0·0	6·0	6·5	7·0	10·0	40·5	2·0	0·0	11·5	0·0	12·5	9·5	0·5	—	—	0·6	Pernicious anæmia in relapse.
XIV	M.	50	5·1	1·4	114	Increased.	0·5	2·5	8·0	8·0	11·5	4·0	0·0	0·0	6·5	0·0	20·5	13·5	11·0	—	—	0·4	Pernicious anæmia in relapse.
XV	M.	70	7·5	1·7	112	Increased.	1·0	1·0	9·0	6·0	6·0	20·0	0·5	0·0	12·0	0·5	27·0	7·5	9·5	—	—	0·4	Pernicious anæmia in relapse.
XVI	F.	65	5·2	1·4	114	Normal.	0·0	1·0	11·0	12·5	7·5	11·5	2·0	0·0	11·5	1·0	28·5	5·5	4·5	—	—	0·6	Pernicious anæmia in relapse.
XVII	F.	70	5·1	1·4	125	Normal.	0·5	2·0	7·0	12·0	12·0	6·0	2·5	0·5	5·5	0·0	30·0	10·5	9·5	—	—	0·4	Pernicious anæmia in relapse.
XVIII	F.	50	5·1	1·2	133	Increased.	0·5	4·5	7·5	5·5	3·0	3·0	1·0	0·0	6·0	0·0	47·0	9·5	12·5	—	—	0·3	Pernicious anæmia in relapse.
XIX	M.	64	4·6	1·1	127	Increased.	2·0	2·0	11·6	7·6	6·4	8·8	2·0	0·4	8·8	0·0	38·4	4·4	6·4	—	—	0·4	Pernicious anæmia in relapse.
XX	F.	55	6·9	1·8	111	Normal.	0·5	2·0	8·0	8·0	13·0	9·5	3·0	0·0	13·0	0·0	26·0	6·0	10·5	—	—	0·4	Pernicious anæmia in relapse.
XXI	M.	55	7·6	2·5	128	Normal.	1·0	0·5	6·0	3·5	10·0	4·5	0·5	0·0	8·5	1·0	10·5	33·5	20·5	—	—	0·2	Pernicious anæmia in relapse.
XXII	F.	62	5·1	1·5	107	Increased.	3·0	2·5	12·0	3·0	3·5	4·0	2·5	0·0	8·5	0·5	39·0	6·0	12·5	0·5	0·5	0·3	Pernicious anæmia in relapse.
XIV	M.	50	14·0	5·1	86	Normal.	1·0	2·0	14·0	8·5	20·0	15·0	1·0	0·0	13·0	5·0	5·0	5·5	7·5	—	2·5	1·4	Pernicious anæmia in remission.
XXIII	M.	60	11·1	3·2	100	Increased.	1·0	2·5	10·0	7·0	14·5	14·0	1·5	0·0	11·5	2·5	5·5	14·5	13·0	—	—	0·6	Pernicious anæmia in remission.
XXIV	F.	55	12·4	4·8	85	Normal.	2·0	3·6	6·0	6·0	13·6	36·4	2·0	0·4	12·0	0·4	2·8	8·4	3·2	0·8	0·4	1·2	Pernicious anæmia in remission.
XXV	M.	62	13·1	4·8	83	Normal.	2·8	3·6	10·8	6·4	19·6	28·4	1·2	0·0	0·0	0·8	3·6	12·4	6·0	—	0·8	1·7	Pernicious anæmia in remission.
XXVI	F.	70	12·2	3·5	114	Normal.	2·0	5·0	13·0	12·0	13·5	18·0	1·0	0·5	7·0	0·7	8·0	12·3	4·0	0·3	1·0	1·3	Pernicious anæmia in remission.
XVIII	F.	50	11·3	3·8	108	Normal.	1·6	3·2	4·0	4·4	15·6	35·2	0·4	0·4	10·4	2·4	3·6	4·4	10·8	1·2	1·6	0·8	Pernicious anæmia in remission.
XXVII	F.	52	11·3	4·8	92	Normal.	0·5	2·0	16·5	7·0	21·5	13·5	0·0	0·5	17·5	2·0	2·5	9·5	5·0	0·5	1·0	1·1	Pernicious anæmia in remission.
XXVIII	F.	51	3·0	0·83	114	Normal.	0·0	0·0	7·0	7·0	16·0	17·0	1·0	0·0	8·0	0·0	27·0	10·0	7·0	—	—	0·3	Pernicious anæmia in remission.
XXIX	F.	75	4·9	1·6	127	Diminished.	1·0	1·0	1·5	7·0	7·0	60·0	1·0	0·5	8·5	1·5	7·0	5·5	2·5	—	—	0·7	Carcinoma of stomach.
XXX	F.	33	9·2	3·0	106	Normal.	1·0	6·0	20·0	17·0	34·0	12·0	1·0	0·0	12·0	3·0	2·0	18·0	8·0	—	—	1·4	Myxœdema.
XXXI	M.	49	6·6	2·0	105	Diminished.	35·0	0·0	1·0	0·0	4·0	6·0	2·0	0·0	23·0	8·0	2·0	8·0	11·0	—	—	1·7	Subleuchæmic leuchæmia.
XXXII	M.	67	5·8	2·0	100	Normal.	4·5	1·5	22·0	17·5	27·5	12·0	1·5	0·5	4·0	4·5	0·0	0·5	2·0	1·0	1·0	18·2	Aplastic anæmia.
XXXIII	F.	61	5·0	1·1	140	Increased.	14·5	22·5	18·5	2·5	2·5	1·0	0·0	0·0	0·0	1·5	2·0	9·5	22·5	—	—	1·7	Carcinoma of the bronchus.
XXXIV	M.	75	10·5	3·0	108	Diminished.	4·5	1·0	8·5	6·5	12·0	34·5	2·0	2·0	7·6	6·5	6·5	4·0	2·0	—	—	1·6	Subleuchæmic myelosis.
XXXV	M.	45	5·2	1·3	123	Diminished.	0·5	0·0	0·5	3·0	5·0	76·0	0·5	0·0	10·0	5·0	0·0	0·5	0·0	—	—	8·0	Splenic anæmia.
XXXVI	F.	48	12·2	3·4	100	Normal.	2·5	2·5	15·0	6·5	7·0	15·5	0·0	0·0	14·0	2·0	1·0	20·5	11·0	1·0	1·5	7·1	*Diabetes mellitus*; *tabes dorsalis*.
XXXVII	F.	45	7·4	1·8	111	Normal.	7·5	5·0	29·5	11·0	18·0	8·0	2·0	0·0	2·5	1·0	0·0	11·0	3·5	1·5	—	3·6	Aplastic anæmia.
XXXVIII	M.	28	7·2	1·6	112	Increased.	0·5	0·0	1·0	2·0	2·0	1·0	0·0	0·0	0·0	0·0	29·5	44·5	19·5	—	—	0·03	Acute erythroblastic anæmia; bronchopneumonia.
XXXIX	F.	56	12·0	3·6	100	Normal.	2·0	2·5	28·0	20·0	16·0	4·0	1·0	0·0	10·0	0·5	0·0	0·5	8·0	1·0	—	6·1	Myxœdema.
XL	M.	37	4·5	1·3	120	Increased.	84·0	0·4	0·6	0·6	0·3	0·0	0·3	0·0	8·3	0·0	0·3	1·3	3·6	0·3	—	16·4	Subleuchæmic leuchæmia.
XLI	F.	56	11·9	4·0	105	Normal.	2·0	1·5	8·5	1·5	8·5	39·5	0·5	0·0	21·0	2·5	3·0	5·5	5·5	—	—	1·0	*Tabes dorsalis*.
XLII	F.	48	3·8	1·1	136	Normal.	1·0	0·0	10·5	7·0	3·5	4·5	1·0	0·0	4·0	0·0	0·5	23·5	44·5	0·5	—	0·2	Idiopathic anæmia.
XLIII	F.	68	9·8	2·1	133	Normal.	0·0	0·0	12·5	9·0	11·5	19·0	3·0	0·0	23·0	2·0	0·0	4·5	5·0	—	0·5	1·1	Sprue.
XLIV	M.	45	1·9	0·8	103	Diminished.	0·8	0·4	3·6	2·4	8·4	22·4	1·2	0·4	42·4	3·2	0·8	4·0	3·2	0·4	2·0	6·9	Aplastic anæmia.
XLV	F.	46	11·9	3·8	105	Normal.	1·0	1·0	15·5	11·0	21·0	6·0	0·5	0·0	12·5	0·0	3·5	15·0	12·0	—	0·5	0·9	Splenic anæmia.
XLVI	F.	?50	11·2	4·0	100	Normal.	0·5	2·0	9·5	9·5	11·5	9·5	1·5	0·5	16·5	0·5	1·0	8·0	0·5	1·0	0·5	2·2	Hæmochromatosis.

TABLE IV.

Case Number.	Sex of Patient.	Age. (Yrs.)	Hæmoglobin Value (Grammes) per 100 Cubic Centimetres.)	Red Cells in Millions per Cubic Millimetre.)	Mean Corpuscular Volume in in Cubic Microns.	Mean Corpuscular Hæmoglobin Content in Micrograms.	Bone Marrow Cellularity.	Results of Differential Cell Count. (Percentages.)														Leucoerythrogenetic Ratio.	Diagnosis.
								Myeloblasts.	Premyelocytes.	Myelocytes.	Young Metamyelocytes.	Band Metamyelocytes.	Neutrophiles.	Eosinophiles.	Basophiles.	Lymphocytes.	Monocytes.	Megaloblasts.	Erythroblasts.	Normoblasts.	Plasma Cells.	Turk Cells.		
XLVII	F.	51	4·0	2·8	62	14	Increased.	3·0	3·0	7·5	5·0	9·9	5·0	1·0	0·5	2·5	0·0	8·5	37·5	17·0	0·0	0·0	0·3	Idiopathic hypochromic anæmia.
XLVIII	M.	49	5·1	2·7	63	19	Normal.	2·0	6·5	12·5	14·0	15·5	12·5	1·5	0·0	8·5	0·0	0·5	8·5	17·0	0·0	0·0	1·3	Idiopathic hypochromic anæmia.
XLIX	F.	48	9·5	4·9	61	19	Normal.	2·0	5·0	6·0	10·0	12·0	30·0	1·0	1·0	11·5	0·0	0·0	11·5	7·0	1·0	0·0	1·2	Idiopathic hypochromic anæmia.
L	F.	45	7·2	4·7	72	15	Normal.	2·5	1·0	6·0	10·5	5·5	24·5	2·0	0·0	23·0	1·0	0·5	9·5	7·0	0·0	0·0	1·1	Idiopathic hypochromic anæmia.
LI	F.	39	6·8	4·7	65	13	Normal.	4·5	2·5	12·5	8·0	13·0	22·0	1·5	0·5	16·5	0·5	1·0	8·0	6·5	1·0	0·5	1·7	Idiopathic hypochromic anæmia.
LII	F.	72	4·4	3·5	57	13	Diminished.	1·5	0·5	6·5	5·0	6·5	43·0	0·5	0·0	19·5	2·0	0·5	6·0	9·0	0·0	0·0	0·9	Idiopathic hypochromic anæmia.
LIV	M.	39	3·5	2·3	65	15	Normal.	1·0	4·0	17·5	14·5	20·0	13·0	0·5	0·0	4·0	2·0	0·0	12·0	5·5	0·0	0·5	2·1	Carcinoma of caecum.
LV	F.	12	6·8	3·2	72	21	Normal.	2·5	1·5	7·0	4·0	12·0	10·5	1·0	0·5	6·5	0·5	5·0	25·5	22·0	1·0	0·0	0·3	Hæmatemesis; splenomegaly.
LVII	M.	33	10·9	5·5	73	20	Normal.	0·8	0·0	10·6	10·8	22·8	16·4	2·0	0·4	8·8	6·0	0·0	4·8	3·2	0·4	0·0	2·7	Pulmonary tuberculosis.
LVIII	M.	51	5·6	4·1	56	14	Normal.	4·0	5·0	9·0	13·0	14·5	21·0	2·0	0·0	8·5	0·0	5·0	9·5	8·0	0·0	0·5	1·3	Carcinoma of stomach.
LIX	F.	61	2·5	1·5	67	17	Normal.	0·0	1·5	9·5	6·0	7·5	48·0	1·0	1·0	17·5	1·0	0·5	2·5	3·5	0·0	0·5	2·9	Jejunal ulcer.

other abnormality was found. A blood examination revealed a hæmoglobin value of 15% (Haldane) and 560,000 red cells per cubic millimetre. One pint of citrated blood was given intravenously and 10 cubic centimetres of "Campolon" were given intramuscularly. Her condition improved and she was discharged from hospital and instructed to attend an out-patient clinic. She did not obey instructions. Four months later her condition was again serious and she was readmitted to hospital. A blood examination revealed a hæmoglobin value of 21%, 830,000 red cells per cubic millimetre and 5,000 white cells per cubic millimetre. A differential count showed that 76% were neutrophile cells, 2% were eosinophile cells, 21% were lymphocytes, and 1% were monocytes.

One pint of citrated blood was given intravenously and two cubic centimetres of "Neohepatex" were injected intramuscularly. A week later another blood transfusion was given and 10 cubic centimetres of "Campolon" were administered intramuscularly. The expected improvement did not occur. It was ascertained that intermittent diarrhœa and constipation had been present for some months previously. Further investigations gave the following information. The Wassermann test elicited no reaction; no abnormality was detected by means of a fractional test meal; the Fouchet test elicited no reaction; the serum calcium content was 7·6 milligrammes per 100 cubic centimetres; the fat content of the fæces was 51·3% (split fat 33·5%). Sternal puncture revealed that 27% of the red cells were megaloblasts.

Death occurred seven weeks after the patient's admission to hospital. Immediately after death 5% formalin in saline solution was introduced into the stomach. A post-mortem examination revealed extensive ulceration throughout the stomach, duodenum, jejunum and ileum (Figures III, IV and V). Œdema of the legs and a bilateral pleural effusion were present. A "thrush-breast" appearance of the heart muscle was observed, and the liver and spleen reacted to the Prussian blue test.

When the patient was first admitted to hospital a diagnosis of pernicious anæmia was made, and this was apparently confirmed by response to treatment with liver extract. Upon her readmission to hospital failure to respond to liver therapy and the results of further investigations disproved the original diagnosis. The presence of steatorrhœa suggested the possibility of non-tropical sprue or Gee's disease. The extensive ulceration of the intestinal tract, revealed at post-mortem examination, explained the cause of the patient's condition as deficient absorption from the small intestine.

Case XXXVIII.—A young man, aged twenty-eight years, complained of dyspnœa on exertion and of anorexia of six weeks' duration. Three weeks before his admission to hospital he had a sore throat, and subsequently his mouth became ulcerated and bleeding occurred from the gums. On examination pronounced facial pallor and ulcerative stomatitis were noted. A blood examination revealed a macrocytic anæmia; the hæmoglobin value was 51%, the red cells numbered 1,600,000 per cubic millimetre, 1% being reticulocytes; and the white cells numbered 4,000 per cubic millimetre. A differential leucocyte count gave the following information: band metamyelocytes, 14%; neutrophile cells, 56%; lymphocytes, 26%; monocytes, 4%. Sternal puncture was performed and it was found that 29·5% of the red cells were megaloblasts. A fractional test meal revealed normal acidity. Neither the Fouchet test nor the Wassermann test elicited a reaction.

Over a period of six weeks the patient was treated with liver extract, ascorbic acid, sulphanilamide and blood transfusion. His condition gradually deteriorated, foul sloughs formed inside the mouth, and an intermittent pyrexia was present until death occurred twelve weeks after the onset of the illness. Two days prior to death a blood examination gave the following information: the hæmoglobin value was 28%, and the red cells numbered 1,100,000 and the white cells 2,500 per cubic millimetre. In the blood film the red cells were well stained and macrocytosis was obvious. There were many nucleated red cells—five erythroblasts and three normoblasts to 100 white cells. A differential cell count gave the following information: band metamyelocytes, 19%; neutrophile cells, 67%; lymphocytes, 12%; monocytes, 2%.

A post-mortem examination was performed and the causes of death were reported as: (i) severe anæmia, (ii) necrotic stomatitis, and (iii) bronchopneumonia. Histological examination of the spleen revealed a predominance of erythropoietic cells and much pigment.

A diagnosis of pernicious anæmia is untenable in this case in view of the patient's age, the presence of normal gastric acidity and failure of response to liver treatment. The cause of the anæmia was unknown and the condition was considered to be analogous to the acute erythroblastic anæmia of childhood.

These two cases of macrocytic anæmia demonstrate that, although megaloblasts are always present in excessive numbers in pernicious anæmia, a megaloblastic bone marrow is not diagnostic of pernicious anæmia.

Microcytic Anæmia.

The results of examination of the blood and of the bone marrow of eleven patients suffering from hypochromic anæmia are set out in Table IV. In all cases a diminished mean corpuscular volume and a low mean corpuscular hæmoglobin level are present. Except in three cases the bone marrow counts reveal a relative diminution in the number of nucleated red cells, and the mean leucoerythrogenetic ratio is 1 : 3; this is less than normal, and indicates a greater leucopoietic than erythropoietic activity. The cellularity of the bone marrow smears was within normal limits except in two cases, in one of which there was an increase and in the other of which there was a decrease in cellularity. Scott[20] has described a particular type of small normoblast with jagged cell outline, polychromatic cytoplasm and pyknotic nucleus, which he regards as characteristic of iron deficiency anæmia. This type of cell was observed in the series of cases of hypochromic anæmia set out in Table IV; but these cells were also observed in other anæmias and in bone marrow smears from the bone marrow of ten normal persons. One cannot therefore accept Scott's contention that a diagnosis of iron deficiency anæmia can be made on sternal puncture findings.

It is concluded that sternal puncture is of no assistance in the recognition of hypochromic anæmia.

Leuchæmia.

Leuchæmia is diagnosed by blood examination, and usually it is not necessary to resort to sternal puncture. In Table V the results of differential counts of bone marrow cells in five cases of myeloid leuchæmia and in three cases of lymphatic leuchæmia are set out. In every case the result of the differential count of bone marrow cells was similar to that of the white cells in the peripheral blood. In Table V the results of counts in five cases of atypical leuchæmia are set out. Two patients (Cases XXXI and LXXI) presented anomalous blood counts with leucopenia, and were tentatively classed as suffering from aplastic anæmia. Examination of bone marrow films revealed a great increase in the number of myeloblasts, suggestive of a leuchæmic condition. At post-mortem examination, apart from manifestation of severe anæmia and a terminal bronchopneumonia in one case, there were no characteristic features. Unfortunately both cadavers were infected with *Bacillus welchii*, and extensive spoiling of the tissues made it impossible to obtain satisfactory histological sections. Thus the tentative clinical diagnosis of subleuchæmic leuchæmia could be neither confirmed nor refuted.

The three other atypical cases were classed as leucosarcoma, and the histories are briefly as follows:

Case LXVIII.—A boy, aged fourteen years, complained of anorexia, weakness and recurrent sweats of two weeks' duration. On examination moderate enlargement of lymph glands, liver and spleen was found. A blood examination revealed a hæmoglobin value of 90%, and 4,500,000 red cells and 156,000 white cells per cubic millimetre. In the blood film a differential cell count showed that 80% of the leucocytes were lymphocytes. In the bone marrow film 80% were lymphocytes and 15% lymphoblasts. Death occurred eight weeks after the boy's admission to hospital. At post-mortem examination a large diffuse tumour growth was found in the anterior mediastinum, and histological examination revealed lymphatic leuchæmic infiltration of the thymus, lymph glands, liver and kidney.

Case LXX.—A man, aged forty-one years, complained of shortness of breath of several months' duration, and also of pain in the left side of the chest and over the sternum. He had lost two stone in weight. On examination facial pallor and signs suggesting pleural effusion were noted. The spleen was enlarged to three fingers' breadth below the costal margin. A blood examination revealed a hæmoglobin value of 45%, and 2,200,000 red cells and 1,200 white

TABLE V.

Case Number.	Sex of Patient.	Age. (Yrs.)	Hæmoglobin Value (Grammes per 100 Cubic Centimetres.)	Red Cells in Millions per Cubic Millimetre.	White Cells in Thousands per Cubic Millimetre.	Bone Marrow Cellularity.	Results of the Differential Cell Count. (Percentages).													Diagnosis.	Leucocyterythro-genetic Ratio.
							Myeloblasts.	Promyelocytes.	Myelocytes.	Young Meta-myelocytes.	Band Meta-myelocytes.	Neutrophiles.	Eosinophiles.	Basophiles.	Lymphoblasts.	Lymphocytes.	Monocytes.	Megaloblasts.	Erythroblasts.	Normoblasts.	Plasma Cells.	Turk Cells.		
LX	F.	57	7·5	2·9	170·0	Increased.	2·0	0·5	26·0	15·0	10·0	21·0	0·5	4·0	0·0	8·0	0·0	0·0	2·0	7·5	0·0	0·0	4·5	Myeloid leuchæmia.
LXI	M.	52	7·9	3·5	86·0	Normal.	6·8	4·5	10·0	13·5	17·5	20·5	1·0	2·8	0·0	6·5	0·5	0·0	6·5	6·5	0·0	0·0	2·4	Myeloid leuchæmia.
LXII	M.	25	8·7	3·2	73·0	Increased.	11·6	7·6	14·4	8·0	21·0	30·4	2·0	2·8	0·0	3·2	1·6	0·0	3·6	0·8	0·0	0·0	6·0	Myeloid leuchæmia.
LXIII	M.	45	6·6	2·1	70·0	Increased.	22·8	11·6	16·0	10·0	12·0	12·0	0·5	2·0	0·0	1·6	0·0	0·0	0·8	0·8	0·0	0·0	4·2	Myeloid leuchæmia.
LXIV	M.	32	6·8	3·0	220·0	Increased.	8·5	3·25	40·0	11·5	7·75	13·5	0·25	0·0	12·75	61·5	1·0	0·0	3·75	1·75	0·0	0·0	16·3	Lymphatic leuchæmia.
LXV	M.	46	12·0	3·5	62·0	Increased.	0·2	0·25	0·25	0·5	0·25	0·25	0·5	0·25	6·3	89·2	0·5	0·0	1·0	0·5	0·0	0·0	0·4	Lymphatic leuchæmia.
LXVI	F.	55	9·7	3·5	100·0	Increased.	0·2	0·0	0·3	0·2	0·2	0·4	0·0	0·0	30·8	28·0	0·8	0·0	21·2	11·2	1·6	0·0	0·6	Lymphatic leuchæmia.
LXVII	M.	28	6·6	2·5	20·0	Increased.	0·2	0·0	1·2	2·0	0·5	0·5	0·0	0·0	15·0	80·0	0·5	0·4	2·0	2·0	0·0	0·0	0·4	Leucosarcoma.
LXVIII	M.	14	13·0	4·5	156·0	Increased.	0·5	0·0	1·2	2·0	0·5	0·0	0·0	0·0	37·0	52·5	0·8	0·0	4·0	0·8	0·0	0·0	0·7	Leucosarcoma.
LXIX	M.	39	4·5	1·3	18·0	Increased.	0·0	0·0	0·5	0·0	0·4	1·6	0·0	0·0	9·6	77·2	0·4	0·0	2·0	0·4	0·0	0·0	0·0	Leucosarcoma.
LXX	M.	41	6·5	2·2	1·0	Increased.	0·0	0·0	0·4	0·8	0·8	0·8	0·2	0·0	0·0	7·4	0·4	0·0	0·2	0·2	0·0	0·0	451·0	Possible subleuchæmic leuchæmia.
LXXI	F.	30	2·2	0·9	2·5	Normal.	88·6	0·4	0·4	0·8	0·8	0·8	0·2	0·0	0·0	23·0	8·0	2·0	8·0	11·0	0·0	0·0	1·7	Possible subleuchæmic leuchæmia.
XXXII	M.	49	6·6	2·0	3·0	Diminished.	31·0	4·0	1·0	0·0	4·0	6·0	2·0	0·0	0·0	0·0	8·0	2·0	8·0	11·0	0·0	0·0		

cells per cubic millimetre. In the differential cell count on a blood film 49% of the leucocytes were found to be lymphocytes and 3% lymphoblasts. A differential count of the bone marrow cells showed that 77% of the leucocytes were lymphocytes and 10% lymphoblasts. The left side of the chest was aspirated and a clear yellow fluid was obtained. Death occurred three weeks after the patient's admission to hospital. The post-mortem examination revealed a diffusely infiltrating tumour of the mediastinum, which extended into the neck. Histological examination of the tumour showed it to be a lymphosarcoma.

CASE LXIX.—A man, aged thirty-nine years, complained of anorexia, weakness, night sweats and loss of weight, of three months' duration. Pleurisy with effusion had occurred two months previously and had developed into an empyema, for which repeated aspirations were made and a rib was resected. On examination a discharging sinus was found in the left side of the chest, and the liver and spleen were reported to be enlarged. At a later date enlargement of the lymph glands occurred. A blood examination revealed a hæmoglobin value of 30%, and 1,300,000 red cells and 18,000 white cells per cubic millimetre. In the blood film 71% of the leucocytes were seen to be lymphocytes and lymphoblasts, while in bone marrow smears 90% were seen to be lymphocytes and lymphoblasts. Death occurred three weeks after the patient's admission to hospital. A post-mortem examination revealed pulmonary tuberculosis and empyema. There was considerable enlargement of the mediastinal and lumbar lymph glands. Histological examination revealed lymphosarcomatosis of lymph glands and extensive lymphoid infiltration of the liver and kidney.

In two cases a mediastinal tumour was present, and in the third case there was considerable enlargement of the mediastinal lymph glands. In all three cases there was a predominance of lymphocytes and lymphoblasts in film preparations of blood and bone marrow. Sternberg[9] introduced the term leucosarcoma to designate those cases of lymphosarcoma in which there was a leuchæmic blood picture. Flashman and Leopold[9] found that in 107 recorded cases of leucosarcoma the primary site of the tumour was in the mediastinum in 60 cases. Parkes-Weber[10] points out that most cases of mediastinal leucosarcomatosis are not recognized as such until post-mortem examination.

In view of the difficulty of accurate clinical diagnosis of leucosarcoma it is held that sternal puncture is a useful procedure, in that the leuchæmic manifestations are more obvious in bone marrow films than in blood films.

Other Blood Diseases.

In Table VI are set out results of the differential cell counts on bone marrow films in several other blood diseases. In four cases of polycythæmia an increase in the number of neutrophile cells is noted, but there are no other findings of significance. It is possible that this increase in the number of mature neutrophile cells may be due to an excessive amount of blood in the aspirated fluid. In two cases of subleuchæmic myelosis no changes of diagnostic importance in films made from the bone marrow were observed. In these cases the diagnosis was made from examination of the peripheral blood, and details of one case have been reported.[11]

In Case XXXIII the original diagnosis was pernicious anæmia. This diagnosis was excluded by a differential count from a smear of the bone marrow, in which no increase was found in the number of megaloblasts. The presence of myelocytes and erythroblasts in blood films suggested the possibility of leucoerythroblastic anæmia associated with carcinoma; and this was confirmed by post-mortem examination, at which a carcinoma of the bronchus was found. One example of acute erythroblastic anæmia is included; the patient was a boy, aged five years. A great increase in the number of nucleated red cells was noted in the film from the bone marrow, and the leucoerythrogenetic ratio was 0 : 9, which indicates greater erythropoietic than leucopoietic activity.

Sternal puncture was performed in six cases of aplastic anæmia. In all cases blood examination revealed a macrocytic anæmia; but in differential counts on films from the bone marrow no increase in the number of megaloblasts was found and a diagnosis of pernicious anæmia was excluded. Sternal puncture is of use in the making of such a distinction, but otherwise reveals no findings which can be regarded as characteristic of aplastic anæmia.

TABLE VI.

Case Number.	Sex of Patient.	Age. (Yrs.)	Hæmoglobin Value (Grammes per 100 Cubic Centimetres.)	Red Cells in Millions per Cubic Millimetre.	White Cells in Thousands per Cubic Millimetre.	Bone Marrow Cellularity.	Results of the Differential Cell Count. (Percentages.)										Diagnosis.	Leucoerythroblastic Ratio.
							Myeloblasts.	Promyelocytes.	Myelocytes.	Young Metamyelocytes.	Band Metamyelocytes.	Neutrophiles.	Eosinophiles.	Basophiles.	Lymphocytes.	Monocytes.		
LXXII	M.	72	20·7	7·4	22	Normal.	1·5	0·0	5·0	8·5	10·0	26·0	4·5	1·0	0·0	3·0	Polycythæmia.	0·4
LXXIII	M.	54	16·4	6·5	10	Normal.	2·0	1·2	10·8	8·8	18·8	30·0	4·4	0·4	11·6	0·8	Polycythæmia.	1·8
LXXIV	M.	—	17·5	6·2	20	Normal.	3·0	1·0	3·0	3·0	3·0	36·0	0·0	1·0	0·0	3·0	Polycythæmia.	0·9
LXXV	M.	40	17·4	9·2	15	Normal.	3·0	0·0	12·0	8·5	15·0	20·0	1·5	0·0	2·0	0·0	Polycythæmia.	0·9
LXXVI	M.	60	11·5	5·5	31	Normal.	3·3	1·3	8·7	5·0	18·6	48·0	2·7	1·0	6·7	0·7	Subleuchæmic myelosis.	5·5
LXXVII	M.	72	10·5	3·0	8·7	Diminished.	4·5	1·0	8·5	6·5	12·0	34·5	2·0	1·0	7·5	6·5	Subleuchæmic myelosis.	1·6
XXXIII	F.	61	6·9	1·1	8	Increased.	14·5	2·5	18·5	2·5	2·5	11·0	2·0	0·0	22·5	6·5	Leucerythroblastic anæmia.	1·3
LXXVIII	M.	5	7·4	2·4	10	Increased.	14·0	2·0	29·0	7·0	5·0	4·0	0·0	0·0	0·0	1·0	Subacute erythroblastic anæmia.	0·9
LXXIX	F.	45	7·9	1·8	11	Normal.	7·5	5·0	29·5	11·0	18·0	8·0	2·0	0·0	2·5	1·0	Aplastic anæmia.	3·6
LXXX	M.	42	7·4	1·8	5	Diminished.	0·8	0·4	3·6	2·4	4·0	22·4	1·2	0·8	42·4	3·2	Aplastic anæmia.	0·8
LXXXI	M.	32	4·4	0·7	6	Diminished.	2·5	0·0	3·5	2·0	3·5	4·0	0·5	0·0	75·0	1·5	Aplastic anæmia.	4·5
LXXXII	M.	40	4·8	1·5	1·6	Normal.	2·5	0·0	20·0	13·5	10·5	6·5	0·5	0·0	4·5	3·0	Aplastic anæmia.	1·2
LXXXIII	M.	67	5·8	2·0	5·6	Normal.	4·5	1·5	22·0	17·5	27·5	12·0	1·5	0·5	4·0	4·5	Aplastic anæmia.	13·0

Sternal puncture was performed in 33 cases of secondary anæmia due to various causes. A differential count on films of the bone marrow revealed no changes of diagnostic significance, and so a consideration of these cases has been omitted.

Summary and Conclusion.

The technique of sternal puncture is described, the simplicity of the method being its greatest recommendation.

There is a wide variation in the results of differential counts of bone marrow cells of normal persons, and the results obtained from a small series of normal subjects agreed with those given by other workers.

Sternal puncture was found to be a useful procedure for differentiating pernicious anæmia from other macrocytic anæmias.

No characteristic findings were demonstrable in a small series of cases of hypochromic anæmia.

A differential count of bone marrow cells was of value in the diagnosis of atypical leuchæmia.

It is concluded that sternal puncture is not to be recommended as a routine procedure in hæmatology; but it is of use in the diagnosis of blood diseases when the findings of ordinary blood examination are anomalous.

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ARGENTAFFIN CARCINOMATA ("CARCINOIDS") OF THE SMALL INTESTINE.

By R. A. WILLIS, M.D., D.Sc., M.R.C.P.,

From the Department of Pathology, Alfred Hospital, and the Department of Pathology, University of Melbourne, Victoria.

THE term "carcinoid tumour", first introduced by Oberndorfer in 1907, has come into general use for the designation of certain small, usually slowly growing, carcinomata of the appendix and of the small intestine. The term is an unfortunate one, as it implies a reputation of innocence which, as later experience has shown, these tumours do not deserve. Kaufmann's statement in his text-book of pathology that "the term carcinoid should not be used, since it is merely an expression of perplexity", is endorsed by the large number of cases now reported in which metastases have developed. In 1926 Stewart and Taylor drew particular attention to the subject of

metastasis of "carcinoid" tumours; and in 1934 I also reviewed some of the reports of cases in which metastases had developed from "carcinoid" tumours of the small intestine and of the appendix. In view of their proclivity to metastasize, these tumours should no longer be spoken of as "carcinoids", but as Kultschitzky-cell or argentaffin carcinomata, since there is abundant evidence that they arise from the specialized epithelial cells of the crypts of Lieberkühn, the yellow cells of Kultschitzky, later called argentaffin cells by Masson.

The term argentaffin, as applied to the Kultschitzky cells and to the tumours derived from them, refers to the presence in the cells of granules which blacken when treated with Masson's ammoniacal silver solution. In most cases, however, these carcinomata are histologically so characteristic that they can be identified without the application of this difficult and somewhat fickle staining method. They typically present well-defined clumps or strands of rather small epithelial cells, uniform in size, polyhedral in shape, and with spherical nuclei of fairly uniform size and appearance with few mitotic figures. The clumps are often solid, but some of them form acini with small glandular lumina.

The argentaffin carcinomata of the small intestine are more prone to produce metastases than are their appendiceal counterparts. In the pathology department of the Alfred Hospital, during the last three years, six cases of argentaffin carcinomata of the small intestine have been seen at autopsy, and in four of these metastases were present. In two of the cases very widely disseminated blood-borne metastases had developed and had occasioned serious diagnostic errors. In another case a small primary growth was accompanied by a very large, probably metastatic, growth in one kidney. Following is an outline of the clinical histories and pathological findings in the six cases.

Reports of Cases.

Case I: Three Argentaffin Carcinomata of the Ileum without Metastases, Discovered Incidentally at Autopsy.

W. McC. (post-mortem examination number 5,669) was a man, aged sixty-six years, who had had repeated hæmorrhages from a chronic duodenal ulcer and who died in spite of repeated transfusions. Post-mortem examination verified the presence of an ulcer, two centimetres in diameter, in the first part of the duodenum, with an eroded bleeding vessel in its base. The mucous membrane of the ileum presented three small, sessile, hemispherical, yellowish tumours, the largest two centimetres in diameter. No metastases could be found. Microscopic examination of these tumours revealed the typical structure of well-differentiated argentaffin carcinoma with both solid and acinar tumour clumps and very few mitotic figures. The tumours lay chiefly in the submucous and mucous coats, but also infiltrated the muscle coat to a variable depth; and in the largest tumour this infiltration reached in places to the serous coat (Figure I).

Case II: Many Argentaffin Carcinomata of the Small Intestine without Metastases, Discovered Incidentally at Autopsy.

J.M. (post-mortem examination number 5,876), a man, aged seventy-seven years, underwent excision of a carcinoma of the sigmoid colon in January, 1939. Microscopically this tumour was an ordinary columnar-celled adenocarcinoma. During the ensuing two months intermittent symptoms of intestinal obstruction appeared, culminating in an exploratory operation early in March, when distension of loops of ileum and some free serous fluid in the peritoneal cavity were found, and some adhesions around the terminal portion of the ileum were divided. The patient died immediately after the operation. Post-mortem examination disclosed the following additional findings. There was an extensive area of myocardial degeneration due to thrombosis of the left coronary artery. The mucosa of the small intestine presented between 20 and 30 small, sessile, hemispherical or flat tumours, most numerous in the ileum, the largest 2·5 centimetres in diameter, with a visible plaque of extension on the peritoneal aspect of the bowel. No metastases either of these tumours or of the original carcinoma of the colon were found. Microscopically the small intestinal tumours were all typical, well-differentiated, argentaffin carcinomata, similar in structure and situation to those of the previous case. In the larger tumours, however, there was more extensive infiltration of the muscle coat, which was, moreover, much thickened, measuring up to six millimetres in width.

Case III: Small Solitary Argentaffin Carcinoma of the Ileum with Multiple Metastases in Lymph Glands and Liver.

K.C. (post-mortem examination number 5,282), a man, aged thirty-seven years, who was admitted to hospital in a semi-comatose state and with signs of left-sided hemiplegia which had come on suddenly some hours previously, died the following day. The responses to the Wassermann tests applied to both blood and cerebro-spinal fluid proved to be strongly positive and the Lange gold curve read "5555552221". Post-mortem examination revealed advanced chronic interstitial nephritis, and a large cerebral hæmorrhage. A firm, slightly pedunculated, yellowish tumour, 1·5 centimetres in diameter, was present in the mucosa of the ileum about nine feet above the ileo-caecal junction, and several adjacent mesenteric glands were hard and enlarged, the largest measuring three centimetres in diameter. Several firm white or slightly yellow nodules were present in the liver, the largest 2·5 centimetres in diameter. Microscopically the bowel nodule, the mesenteric glands, and the liver nodules all showed the typical structure of well-differentiated argentaffin carcinoma. Although to the naked eye the intestinal growth had appeared to be restricted to the mucous and submucous coats, microscopically there was a fine widespread infiltration of the muscle and serous layers beneath the tumour, and the infiltrated muscle coat was thickened to double or treble its normal width. Although the metastases in the lymph glands and liver had attained a much greater bulk than the primary tumour, their microscopic structure was no less typical, mitotic figures were few, and many parts of the growths had an abundant fibrous stroma (Figure II).

Case IV: Small Solitary Argentaffin Carcinoma of the Ileum with Extension to an Adjacent Lymph Gland and a Huge Solitary, Probably Metastatic, Growth in One Kidney.

V.S. (post-mortem examination number 5,391) was a man, aged sixty-seven years, who was admitted to hospital in June, 1937, with ulcerated eczematous legs. This condition improved; but towards the end of July abdominal distension appeared and gradually became worse. Post-mortem examination revealed a large, irregularly lobulated, yellowish tumour, about 600 grammes in weight, replacing most of the left kidney. The intestines were much distended and general fibrino-purulent peritonitis was present. In the terminal portion of the ileum, five centimetres above the ileo-caecal valve, there was a firm, pedunculated, yellowish growth, two centimetres in diameter, projecting into the lumen and attached to the bowel mucosa by a pedicle two centimetres long. This growth had acted as a ball-valve at the ileo-caecal orifice, in which it lay. Examination of the peritoneum external to this area revealed slight nodular induration over a patch one centimetre in diameter, and an adjacent lymph gland was hard and slightly enlarged. A post-mortem diagnosis of primary carcinoma of the kidney with a solitary metastasis in the bowel was made. Subsequent microscopic examination, however, surprisingly showed that the reverse was probably the case. The tumour in the ileum and its extension in the adjacent mesentery and lymph gland showed the typical structure of a well-differentiated argentaffin carcinoma. The kidney tumour, though less typical, appeared to be of the same nature, consisting of clumps of small polyhedral cells with dark rounded nuclei similar in appearance to those of the bowel tumour (Figure III). The tumour clumps were not so sharply defined as in the primary growth, and the cytoplasm of the cells was slightly more abundant and less darkly stained. Mitotic figures, as in the intestinal tumour, were scanty. The tumour showed no resemblance to the usual clear-celled papillary adeno-carcinoma of the kidney, and, although complete proof of its nature cannot be advanced, the conclusion was reached that it was probably a metastasis of the intestinal growth.

CASE V: *Multiple Argentaffin Carcinomata of the Small Intestine with Metastases in Liver, Lungs, Kidneys, Adrenals, Gall-Bladder, Stomach, Pancreas, Retroperitoneal Tissues, Subcutaneous Tissue and Many Groups of Lymph Glands.*

H.B. (post-mortem examination number 5,919), a man, aged fifty-six years, was admitted to hospital in April, 1939, with the diagnosis of "carcinoma of the kidney". He gave a history of attacks of pain in the right upper lumbar region and abdomen during the previous four months, and he had also lost about one stone in weight. He had attended a public hospital where renal calculus was suspected, but skiagrams failed to reveal any stones. Three weeks before his admission to hospital his private doctor had discovered

a tumour in the right loin. Examination disclosed a large rounded mass in the loin, an enlarged firm gland in the right side of the neck, and two subcutaneous masses, each about the size of a hen's egg, situated on either side of the mid-line, about the level of the first lumbar vertebra. The patient died four days after his admission to hospital. Post-mortem examination disclosed the following relevant abnormalities. The right lung contained a brownish mottled mass of growth five centimetres in diameter situated in the middle of the lower lobe. A similar tumour, two centimetres in diameter, was present in the upper lobe of the left lung. The liver contained many rounded secondary tumours measuring up to three centimetres in diameter, consisting of white tissue with mottled brown or slate-coloured centres. The gall-bladder contained a single pedunculated pigmented tumour six millimetres in diameter. Both adrenal glands were replaced by large soft tumours, each about 12 centimetres in diameter, consisting partly of white and partly of mottled brown or grey tissue; the tumour from the right side contained a cystic area with brownish fluid contents. A similar large cystic and pigmented tumour, about 15 centimetres in diameter, lay in the retroperitoneal tissue just below the right kidney. Both kidneys contained scattered small secondary growths, white or grey in colour, and situated chiefly in the cortex. The mucous membrane of the small intestine presented many small sessile or pedunculated tumours, consisting of white, yellow or greyish tissue, and situated in both the jejunum and the ileum. The largest of these tumours, about three centimetres in diameter, was situated near the middle of the small intestine and had caused obstruction by an intussusception eight centimetres in length. The mucous membrane of the stomach presented two small flat tumours, each six millimetres in diameter, with central crateriform ulcers. Several small white or grey tumours were present in the pancreas. Many mesenteric, mediastinal and cervical lymph glands contained white or grey tumour deposits, and the subcutaneous masses in the lumbar region also consisted of growth. Careful examination failed to reveal any tumours in the heart, œsophagus, trachea, thyreoid, brain, eyes, orbits, skin, large intestine, spleen, bladder, prostate, testes, vertebræ, skull or ribs. An initial post-mortem diagnosis of disseminated melanoma was made, though some hesitation was felt regarding this diagnosis because of the absence of any demonstrable primary tumour in the skin or eyes. An idea was entertained of a possible primary adrenal origin. Microscopic study, however, showed that parts of the intestinal tumours and of those in the liver, kidneys and lymph glands had the structure of unmistakable argentaffin carcinoma (Figure IV). In other parts of both the intestinal and metastatic tumours, however, the tissue was anaplastic, presenting masses of undifferentiated polyhedral, spindle-shaped or giant tumours cells, arranged either in irregular clumps or quite diffusely, and containing many mitotic figures (Figure V). Transitions between the well-differentiated and the more anaplastic growth were evident. The intestinal growth involved the mucous and submucous coats only; nowhere was the muscle coat invaded. The pigmentation of the tumours was clearly due not to melanin, but to extravasated blood, since areas of necrosis and hæmorrhage were present and the pigment lay in the tissue interstices or was contained within wandering phagocytic cells. The tumour cells were not pigmented.

Case VI: Multiple Argentaffin Carcinomata of the Jejunum with Metastases in the Brain, Pancreas, Mesentery and Skin.

B.M. (post-mortem examination number 6,336), a man, aged forty-one years, was admitted to hospital in March, 1940, with the diagnosis of "cerebral tumour". For three months previously he had suffered from mental confusion, speech defects, headache and ataxic gait. Bilateral papilloedema was present and the cerebro-spinal fluid pressure was high. Neurological and ventriculographic examination pointed to a tumour of the left cerebral hemisphere, and at operation a cystic tumour of the temporal lobe was removed. Immediate microscopic examination of the tissue unexpectedly disclosed secondary carcinoma. The patient died four days after the operation. Post-mortem examination disclosed several further tumours in both cerebral hemispheres, most of them subcortical in situation, and the largest 1·5 centimetres in diameter. The mucous membrane of the jejunum presented 50 or 60 tumours, varying from the size of a pin's head up to two centimetres in diameter, and either sessile and flat or rounded and slightly pedunculated. In several of the larger tumours surface ulceration was present. On section the tumours were white or slightly yellow in colour, and nowhere involved the muscle coat of the bowel. The ileum and the large intestine contained no tumours. Several small white tumour nodules, the largest eight millimetres in diameter, were present in the pancreas. A single small nodule of growth was found in the mesentery. The skin of the lateral wall of the right axilla contained a small white nodule, four millimetres in diameter. Thorough examination failed to discover any tumours in the heart, lungs, thyreoid, œsophagus, trachea, meninges, pituitary, orbits, eyes, internal and middle ears, nasal cavity, paranasal sinuses, Eustachian tubes, salivary glands, liver, gall-bladder, bile ducts, spleen, adrenals, stomach, kidneys, bladder, prostate, testes, vertebræ, ribs or skull. Microscopic study showed the intestinal tumours to have the structure of fairly cellular but unmistakable argentaffin carcinoma; and the growths in the pancreas, brain, skin and mesentery, though rather more active and less typical, were clearly of the same nature (Figure VI).

Discussion.

Adequate general accounts and reviews of the subject of argentaffin carcinoma of the small intestine are afforded by the papers of Cope and Newcomb (1930), Cooke (1931), Marangos (1931), Humphreys (1934), and Ariel (1939), which render further comprehensive review unnecessary. The object of the present paper is rather to stress the malignancy and metastatic propensities which these tumours may display and the diagnostic difficulties they may occasion to the pathologist as well as to the clinician, and to draw attention to one or two features which, I believe, have not previously been commented on.

Malignancy and Metastases.

Of the six cases described in this paper, metastases were present in four. In Case III the metastases were restricted to the regional lymph glands and liver; in Case IV a large solitary, probably secondary, growth was present in the kidney; and in Cases V and VI multiple remote blood-borne metastatic growths were present. These findings denote a high degree of malignancy and show the falsity of the implication of innocence in Oberndorfer's name "carcinoid" tumour; the tumours are frank carcinomata, sometimes extremely malignant carcinomata. An insufficiently recognized point, which is well exemplified in all four cases with metastases, is that very small, often symptomless, primary tumours may nevertheless produce bulky, clinically obtrusive metastases. Indeed, unless the intestines are opened and carefully examined at autopsy, the primary intestinal growths in many cases may easily escape discovery. In the six cases described above the diameters of the tumours (the largest being taken in the cases with multiple growths) were 2·0, 2·5, 1·5, 2·0, 3·0 and 2·0 centimetres respectively.

Difficulties in Pathological Diagnosis.

Even after complete post-mortem examination the nature of a case may remain obscure unless thorough histological study is undertaken. This is particularly well illustrated in Cases V and VI. In Case V the grey and brown pigmentation of many of the bulky metastatic tumours suggested that the condition was one of widely disseminated melanomatosis, and perplexity was felt that no primary melanotic tumour was present in the skin or eyes. Even after preliminary histological study the nature of the tumour remained obscure, and it was only after many sections had been examined that the identity of the growth was at last realized. Had sections of only the more anaplastic parts of the growths been examined, the real nature of the disease would have escaped recognition; and, for lack of a better interpretation, the case might have been diagnosed as one of primary visceral melanoma. Case VI also caused initial difficulty in the post-mortem diagnosis. Sections of surgically removed pieces of the cerebral growth had shown unmistakable carcinoma, and it was expected that autopsy would disclose a primary growth in one of the usual situations—lung, kidney, thyreoid or elsewhere. At autopsy the multiple small intestinal tumours were thought to be, like the cerebral ones, metastatic growths; and some perplexity was felt when careful search failed to disclose any primary growth in one of the more usual sites. It was only when microscopic study proved the intestinal tumours to be argentaffin carcinomata that these were recognized as the source of the metastatic tumours. I believe this to be the first reported case of metastases in the brain from argentaffin carcinoma.

The Nature of the Pancreatic, Gastric and Biliary Tumours.

In Cases V and VI the pancreas contained multiple small growths, and in Case V tumours were present also in the mucous membranes of the stomach and gall-bladder. These have been provisionally described above as metastatic. While I think it probable that this view is correct, there is an alternative interpretation which cannot, in our present state of knowledge, be excluded—namely, that some or all of the pancreatic, gastric and biliary tumours, like the intestinal tumours, may have been multiple primary formations. While our knowledge of the distribution of argentaffin cells is still not precise, they are believed to occur in the stomach, and in an admirable paper Kerr and Lendrum (1936) record their presence in a papilloma of the gall-bladder and note that Patzelt found them also in the pancreatic and biliary ducts. In cases in which multiple argentaffin growths arise in the intestine, as in our Cases V and VI, it is theoretically quite possible, therefore, that tumours may develop simultaneously from argentaffin cells in other situations—the stomach, the biliary tract and the pancreas. In this connexion, review of a case which I reported in 1936 as "a rare type of diffuse carcinoma of the pancreas with unusual metastases" is also of interest. In this case, in addition to clearly metastatic growths in the liver, heart and thyreoid, multiple intestinal tumours were present, and in the pancreas widespread cancerous replacement was evident. The structure of the intestinal tumours was described and depicted as closely resembling that of the usual "carcinoids"; but, in view of the large size and diffuse character of the pancreatic tumour, it was concluded that this was primary and that the intestinal growths were metastatic. I now think this conclusion to have been in part erroneous. While I still believe it probable that the pancreatic tumour was a primary growth in that organ, reexamination of the specimens in the light of the later experiences described in the present paper satisfies me that the intestinal tumours were multiple primary argentaffin carcinomata; and I think it quite likely that the case was one of multiple argentaffin growths simultaneously affecting the intestines and pancreas. It may be added, in conclusion, that the conception of multifocal growths arising over a wide field of a particular tissue is by no means new. This is not unusual, for example, with rodent carcinomata of the skin, carcinoma of the breast, and papillary tumours of the urinary tract. It appears clear in such cases that the carcinogenic stimulus, applied over an extensive field of similar tissue, has evoked multiple tumours in various parts of that field. We have no knowledge of the nature of the stimulus responsible for the development of argentaffin carcinomata, nor are we likely to possess such knowledge until we know something of the functions of argentaffin cells.

Summary.

1. Six post-mortem cases of argentaffin carcinoma of the small intestine are described.

2. The malignancy of these tumours and their capacity to metastasize are stressed.

3. The difficulties of pathological, as well as clinical, diagnosis which the tumours may occasion, are pointed out.

4. It is considered possible that tumours found in the pancreas, biliary tract or stomach of subjects with multiple intestinal growths, may be not metastases, but multiple primary formations.

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Legends to Illustrations.

(See Special Plate.)

FIGURE I (Case I). Section of the bowel wall, showing typical argentaffin carcinoma occupying the submucosa, finely infiltrating the muscle coat and forming clumps in the subserous tissues. × 32.

FIGURE II (Case III). Metastatic growth in the liver, showing the typical structure of argentaffin carcinoma. × 80.

FIGURE III (Case IV). Microscopic appearance of the renal growth, showing cytological resemblance to argentaffin carcinoma. × 200.

FIGURE IV (Case V). Metastatic growth in the liver, showing typical structure. × 105.

FIGURE V (Case V). Part of intestinal growth, showing atypical spindle-celled structure. × 105.

FIGURE VI (Case VI). Structure of a cerebral metastasis of argentaffin carcinoma. × 95.

THE SCHICK REACTION: STABILIZED TOXIN COMPARED WITH TOXIN DILUTED IN SALINE SOLUTION.

By HAROLD WILSON[1] and N. E. GOLDSWORTHY.

From the Kolling Laboratory, Royal North Shore Hospital of Sydney, and the Department of Bacteriology, University of Sydney.

DIPHTHERIA toxin loses potency so rapidly when diluted with physiological saline solution that diluted toxin for the Schick test has to be prepared freshly each time it is required. To overcome this disadvantage many attempts have been made to devise a diluent which will permit of the storage of diluted toxin without diminution of strength. This work has been reviewed by Taylor and Moloney (1939).

Toxin diluted ready for use in the diluent recommended by Adey and Patterson (1937) was tested by Merrillees (1937) on about 5,000 children and found satisfactory. Toxin so diluted remained stable at 30° to 40° C. for thirty days, and for much longer at lower temperatures. The diluent is a solution of purified gelatin in borate buffer.

This paper is a report upon the reactions which followed the injection of (i) stabilized toxin and (ii) the same toxin diluted in physiological saline solution (the orthodox preparation).

Materials.

The toxin was made in July, 1934, and designated 459E. It fulfilled standard requirements; its toxicity was relatively low, whereas its combining power was relatively high.[2] The tests here reported were carried out between

[1] Working under grants from the Commonwealth Government and from the National Health and Medical Research Council of Australia.

[2] The Lf dose, as estimated at the Commonwealth Serum Laboratories in November, 1939, was 0·1 millilitre; that is, the toxin contained 10 antigenic units per millilitre, floccules appearing in fifty-five minutes at 50° C. The Lr/1,000 dose, as estimated by us, was 0·00027 millilitre; 0·2 millilitre of toxin diluted to 1 in 600, further diluted 1 in 25, caused redness in two out of three guinea-pigs when injected into the skin.

April and November, 1939, and during that time the undiluted toxin deteriorated so that the amount of toxin constituting one Schick test dose in a volume of 0·2 millilitre was increased from 1/3,600 millilitre to 1/3,075 millilitre; that is, the dilution fell from 1 in 720 to 1 in 615.

Immediately before use toxin was suitably diluted in (*a*) 0·85% sodium chloride solution and (*b*) the diluting fluid of Adey and Patterson. In about half the tests this second (*b*) dilution was prepared for us at the Commonwealth Serum Laboratories from the same toxin, 459E. A portion of each diluted toxin was heated at 90° C. for fifteen minutes to serve as a control.

Methods.

Schick Tests on the Human Subject.

When the Schick test was being carried out on the human subject care was taken to ensure that a proper dose was given; dead space in the needle was eliminated by the ejection of 0·1 millilitre of fluid from the syringe before the needle was inserted into the skin. In each instance 0·2 millilitre of toxin diluted in buffered gelatin solution was injected into the skin of the right forearm and 0·2 millilitre of toxin diluted in saline solution was injected into the skin of the left forearm. The control injections were given in the corresponding forearms distal to the test injections. The results were read on the fourth and seventh days (the day after the injections being counted as the first) or more often. The size and character of reactions were carefully recorded.

No attempt was made to observe and compare the results in a large number of persons; it was thought better to spend time and care in injecting the toxin, in making accurate observations and in keeping full records of the results in comparatively few individuals. The total of 447 individuals comprised 96 children, 112 probationer nurses and 239 undergraduates among whom were included a few young resident medical officers and laboratory workers; none of these 447 subjects had had diphtheria and none had been immunized against it.

Experiments on Rabbits.

The following experiment was carried out in an endeavour to throw light upon the cause of some interesting differences (mentioned below, under "Results") between the reactions which followed the injection of toxin diluted in saline solution and of toxin diluted in buffered gelatin solution.

Amounts of toxin ranging from $^1/_{25}$ of a Schick test dose to five Schick test doses were diluted in (i) the buffered gelatin solution of Adey and Patterson and (ii) physiological saline solution and injected, in a volume of 0·2 millilitre, intradermally at corresponding points on opposite sides respectively of each of four rabbits. The resulting skin reactions were measured daily.

Results.

Observations on Schick Tests on the Human Subject.

Among the 447 subjects in whom the results of the injection of toxin diluted in saline solution were compared with the results of injecting the same toxin diluted in buffered gelatin solution the results were as follows:

Readings agreed:		
"Positive"	238	431
"Pseudo" and "positive"	8	
"Negative"	158	
"Pseudo" and "negative"	4	
"Protein reactors"[1]	23	
Readings differed:		
"Positive" with dilution in saline solution, "negative" with dilution in gelatin solution	11	16
"Negative" with dilution in saline solution, "positive" with dilution in gelatin solution	5	
Total		447

[1] "Protein reactors" were persons who gave a reaction at both sites (toxin and control). This reaction persisted for ten days or more and faded equally slowly at both sites.

The readings agreed in 431 subjects, but differed in 16 subjects (3·6%). In 11 of these 16 subjects the reactions were read as "positive" when the toxin was diluted in saline solution, but "negative" when the toxin was diluted in buffered gelatin solution, and as the reverse in five subjects. Similar results are recorded by Thelander (1933), who, after determining the amount of antitoxin in the blood, concluded that the toxin diluted in saline solution was more reliable than stabilized toxin.

Although qualitatively the results of injecting toxin diluted in either of the two fluids were the same in 96·4% of subjects, quantitatively the reactions themselves often differed. In other words, two undeniably positive reactions in one subject were sometimes very different in size or intensity. Generally the reaction which followed the injection of toxin diluted in saline solution was smaller but more intense than the reaction which followed the injection of toxin diluted in buffered gelatin solution; this was apt to be comparatively diffuse and pale, giving the impression that it was the weaker reaction. Also, as shown in Figures I and II, this reaction often had a pale centre with, by contrast, a more intensely red periphery, whereas that reaction which followed the injection of toxin diluted in saline solution often had a comparatively intensely red centre. The moderate or strong reactions with both test fluids were easy to read; but generally the weak reactions with the toxin diluted in saline solution were rather easier to read than the weak reactions with the toxin diluted in buffered gelatin solution. It was usually easier to see a relatively small dark reaction than a relatively large pale one which was apt to be vague.

Another difference was that the skin reactions which sometimes appeared a few minutes after the injection and faded some hours later were more frequent and stronger with the toxin diluted in buffered gelatin solution than with the toxin diluted in saline solution.

No reaction was observed to follow the injection into more than 100 individuals of the gelatin solution alone (that is, without toxin), either heated at 90° C. for fifteen minutes or unheated.

Results of the Experiments on Rabbits.

The four rabbits injected with various quantities of toxin all showed similar reactions. The dimensions of the reactions in one animal are set out in Table I and the figures indicate that the reactions with toxin in buffered gelatin solution were wider than those with toxin in physiological saline solution. With the weaker reactions the toxin in buffered gelatin solution caused paler and less distinct reactions than those caused by the toxin in saline solution.

TABLE I.

The Size of the Reactions which Followed the Intradermal Injection in the Rabbit of Diphtheria Toxin Diluted (i) in Buffered Gelatin Solution and (ii) in Physiological Saline Solution.

Schick Test Doses.	Size of Reaction. (Millimetres.)	
	Right Side of Rabbit: Toxin Diluted in Saline Solution.	Left Side of Rabbit: Toxin Diluted in Gelatin Solution.
5	21×21	29×24
1	17×15	20×18
$\frac{1}{5}$	13×13	19×16
$\frac{1}{25}$	6×6	16×16

Discussion.

Our results appear to have differed in two respects from the results recorded by Merrillees (1937):

1. Merrillees reported that, with the toxin diluted in buffered gelatin solution, doubtful readings were almost eliminated. Dwyer (1938) reported similarly. We have obtained more doubtful readings, particularly with the

weak reactions, with toxin so diluted than with toxin diluted in saline solution.

2. Merrillees reported also that the reactions which followed the injection of toxin diluted in buffered gelatin solution were nearly constant in area, being about 20 millimetres in diameter. We, like Dwyer (1938), observed them to vary widely in area, ranging from five to more than 50 millimetres in diameter. These reactions varied more widely than those caused by toxin diluted in saline solution.

The greater area of the reactions caused by toxin in buffered gelatin solution as compared with the reactions caused by toxin in saline solution would seem to be related to the power possessed by some fluids of causing dispersion through the skin of substances with which the fluids are mixed. In some work (Wilson, 1939) on bacterial spreading factors (Duran-Reynals, 1933, 1935) it was noticed that substances which were injected into the skin together with tap-water, broth or serum-broth spread more widely than the same substances injected together with physiological saline solution. As shown in Table I, similar results were obtained when the area of the reaction which followed intradermal injection into the rabbit of diphtheria toxin diluted in buffered gelatin solution was compared with the area of the reaction which followed injection of the toxin diluted in physiological saline solution. These results in rabbits resembled the results with the two diluents in the human subject. Thus the strong or weak reactions which followed the injection into the rabbit of various amounts of toxin resembled the reactions in human subjects who reacted strongly or weakly respectively to the Schick test. It is not known why some fluids possess this power to cause dispersion in the skin (Aylward, 1937, Medinaveitia, 1939).

Summary.

The reactions which followed the injection of Schick toxin diluted in either physiological saline solution or the buffered gelatin solution of Adey and Patterson have been compared in 447 subjects. The results agreed in 96·4% of subjects.

The reactions caused by toxin in saline solution were generally smaller and more intense than the reactions caused by toxin in buffered gelatin solution which were apt sometimes to be comparatively diffuse and vague.

The lesion which followed the intradermal injection into the rabbit of diphtheria toxin diluted in the buffered gelatin solution was larger than the lesion which followed the injection of an equal amount of the same toxin diluted in saline solution. In this respect the buffered gelatin solution resembled some other fluids which had been compared with saline solution in experiments with the spreading factor of Duran-Reynals.

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Legends to Illustrations.

(See Special Plate.)

FIGURE I. Photograph (one-tenth greater than natural size) of the skin reaction to the Schick test on the fourth day after injection; right arm; toxin diluted in gelatin solution. Diffuse redness with central pallor; outside measurement, 40 × 30 millimetres.

FIGURE II. Skin reaction (one-tenth greater than natural size) on the left arm of the same subject, four days after injection; toxin diluted in physiological saline solution. Redness relatively more intense at the centre; outside measurements, 28 × 20 millimetres.

SOME SURGICAL PANCREATIC DISEASES.[1]

By T. M. FURBER,
Sydney.

SYSTEMATIC descriptions of all aspects of pancreatic disease are readily available, so I thought that some more or less random personal impressions would perhaps be at least not so dry as a rehash of easily ascertained information.

In the bodily economy the pancreas is of the highest import, producing not only its marvellous internal secretion, but also powerful digestive enzymes and such an active chemical reagent as sodium bicarbonate. The abundance of its threefold blood supply and the high coefficient of oxidation which it shares with such active glands as the kidney and salivary apparatus, both mark it out as a very busy factory. By an all-wise Providence this notable gland has been cradled behind the peritoneum in a cosy nook, where it is protected from infection spreading by way of the peritoneum and where it is also relatively safe from injury.

From a surgical point of view the pancreas is usually well behaved and carries out its duties with exemplary regularity and prudence. At the behest of the vagus it produces a juice rich in the immediate precursors of three potent digestive enzymes, and in response to secretin the juice is watery, abundant and rich in sodium bicarbonate.

Trypsinogen is a substance of great potential chemical energy, and, like a Mills bomb with the pin in, it is quite harmless; but when the pin is withdrawn by enterokinase or some abnormal activator it becomes a very active chemical reagent. It is but seldom that the pin comes out prematurely; but when it does there follows a devastating explosion which we call acute hæmorrhagic pancreatitis, one of the most dramatic and rapidly fatal of the abdominal catastrophes.

I well remember a man at Sydney Hospital who, while waiting in Dr. Hamilton Marshall's out-patient department, fell from his seat, labouring under what Lord Moynihan has so aptly called "illimitable agony". It was evident even to such mole-eyed students as we were that the unfortunate old man was stricken unto death, as he quickly became a dreadful, livid, ashen hue, and writhed and groaned in a calamity of pain, fighting for breath and calling on our Maker for help in what was truly his last extremity. Some three days later he died, as was discovered at autopsy, of pancreatic necrosis.

[1] A post-graduate lecture delivered on August 4, 1940, at the Prince Henry Hospital, Sydney.

Another picture which comes to mind is that of a decent, middle-aged widow, who lived virtuously alone with gall-stones, which for years, in spite of advice, she had harboured and, I think, cherished. Soon after dinner one night she was overwhelmed by an abdominal cataclysm. When I saw her a few hours later she was sitting up in the middle of a big double bed, slowly rocking herself back and forth and gently moaning, but not taking the slightest notice of the bewildered females who clucked and fluttered around her, nor answering direct questions, for her sensorium was apparently saturated by the tremendous discharge of afferent stimuli from her abdomen. Knowing that she had gall-stones, I guessed that she had acute pancreatitis, and advised her immediate removal to hospital; but while arrangements were being made her tempestuous daughter burst in on us like a southerly gale and whisked the unfortunate old lady to her own home, where the poor soul perished of what was proved at the coroner's autopsy to be pancreatic necrosis.

Fortune seemed to smile on a sprightly, brisk, young bachelor when he won the lottery. He at once gave up his uninteresting and comparatively unremunerative toil for what was for him the more congenial task of helping the brewery proprietors to issue a few more bonus shares. He succeeded so well in this no doubt laudable crusade that for a month or more he was seldom sober and thought he was having a wonderful time, till suddenly the Grim Reaper breathed on his pancreas and it died, and so did its owner within three days. He, unlike the other two, lay as still as a mouse or as a patient with a ruptured peptic ulcer. The metabolic revolution had caused such profound shock that, as Professor Wilson used to say, "it was patent to the meanest intelligence" that the poor fellow was destined soon to find out whether the story of Saint Peter and the Digger had any truth in it. Resuscitatory treatment did not reclaim him, and he died without operation. Autopsy revealed hæmorrhagic pancreatitis.

Cases of the gravity of these three may well be likened to the detonation of a metabolic Mills bomb; but many more occur in which the explosion is rather of the order of that of a basket bomb so beloved by first-year students, which causes much noise but little damage, so that wisely directed non-operative treatment is effective; while others again are just squibs, as when a few areas of fat necrosis or limited œdema round the pancreas are unexpectedly found during an operation for gall-stones.

Recent opinion suggests that minor attacks of pancreatitis are not uncommon, and that they are at the bottom of a number of vague slight illnesses which are put down to "digestive upsets".

As cases of all degrees of severity may occur, the symptoms and signs are naturally variable; but almost all have this in common, that they are seldom diagnosed before operation or autopsy because what is thought to be an uncommon condition is not considered. But in fulminating cases it does not take much clinical acumen to realize that some major catastrophe has occurred, such as acute perforation of a hollow viscus (ulcer or diverticulum), or a lesion which has compromised the blood supply of a large section of the bowel (such as mesenteric thrombosis or a volvulus), or a coronary thrombosis or acute irritant poisoning; and when the field is so narrowed down careful thought should allow one to pick the winner.

In the less severe cases diagnosis is admittedly difficult; but if pancreatitis is suspected when other commoner lesions of the upper part of the abdomen cannot be confidently diagnosed, fewer mistakes will be made.

I have no personal experience of the value of the diastase test on urine or serum, or both; but whenever it is mentioned in the current literature it is almost always commended as being very reliable.

It would appear that the blood sugar level is very often raised, a fact which should help to distinguish acute pancreatitis from its competitors in the diagnostic race. The interesting observation has been but lately made that if the duodenal fluid obtained from a Ryle's tube is examined it will be found that the quantities of lipase, trypsin and amylase are diminished in that order.

These tests are no doubt helpful; but I feel that clinical acumen will still be the surest guide to our faltering steps in the diagnostic maze.

While speaking of diagnosis I should like to mention that the patchy blue discoloration described is not characteristic of pancreatitis, as it occurs in the late stages of peritonitis or intestinal obstruction; for after all it is merely a sign of advanced peripheral circulatory failure—a sort of ante-mortem suggillation, if I may be permitted the term. Though I have looked for it, I have never seen the extravasation of blood in the costo-vertebral angle or in the epigastric or umbilical regions as described in the books.

Pathogenesis.

It is generally agreed that in some way the trypsinogen is activated into trypsin, which in turn causes digestion of the pancreas and surrounding tissues, so that the blood is flooded with highly poisonous split protein products; but when it comes to the making of a decision as to what activates the trypsinogen, the pundits are at variance. Regurgitation of infected bile has provided a convenient explanation ever since Opie, that Colossus of the pancreas, found in 1901 a stone impacted in Vater's papilla in a case of pancreatic necrosis. Going further into the matter, he satisfied himself that in 75% of cases the anatomical arrangements of the terminations of the pancreatic and common bile ducts were such that reflux was possible. Mann and Giordano, however, proved to their satisfaction that in 95% of bodies a stone impacted in Vater's papilla would also block the pancreatic duct. Noble and Cameron returned to the charge and were convinced that in 65% of cases bile would flow into the pancreatic duct if a stone were caught in the papilla. Further confusion is injected by Bernhard, who, in cases in which the common duct had been drained with a T-tube, found that in 10% radio-opaque fluid could be injected through the tube into the common duct and up into the pancreatic duct, and that in a given patient this occurred at some times and not at others; yet these people did not have or contract pancreatitis.

Again, the pancreatic juice is secreted at a much higher pressure than is bile, so that if it were possible to convert the bile and pancreatic ducts into a closed system, pancreatic juice should flow into the common duct and not *vice versa*.

Two other attractive theories have been put forward, but in both there are a number of assumptions which are capable neither of proof nor of disproof. Archibald, in order to account for the great number of cases of pancreatitis in which no stone was found in the papilla, postulated spasm of the sphincter of Oddi similar to the pylorospasm which we know is often associated with gall-stones. The other equally nebulous idea supposes that as a result of chronic pancreatitis fibrosis occurs round the ducts and that metaplasia and accumulation of epithelium occur in the ducts, both leading to a certain amount of blockage. It is then supposed that the rush of juice after a heavy meal is banked up so that some of the acini rupture and trypsinogen is activated by the tissue juices. Whether this is true or not, it is worth remembering, for it is a fact that pancreatitis is apt to occur after a heavy meal; German writers themselves have drawn attention to its frequency in Germany in the gluttonous years before the Great War and to its comparative rarity during the war. This fact also draws attention to the necessity in conservative treatment of severely limiting the food intake so as to give the pancreas physiological rest.

Treatment.

The accepted treatment in these fulminating cases has been to enter the mass by blunt dissection with the idea of relieving tension and so limiting the spread of the gangrene, and then to put in a tube to drain away the poisonous split protein products; it is generally recommended then to drain the gall-bladder. On the few occasions that I have done this, it has been abundantly clear that I have failed in both objects, and reference to some anatomical points will show the reasons. To begin with, the pancreas is six inches long, and it surely seems too much to expect one tube in a coarsely lobulated organ to drain more than a very small area. Now the pancreas has such a thin capsule that with the naked eye it is hard to see; but the organ is cut up into a number

ILLUSTRATIONS TO THE ARTICLE BY DR. JOHN A. McLEAN.

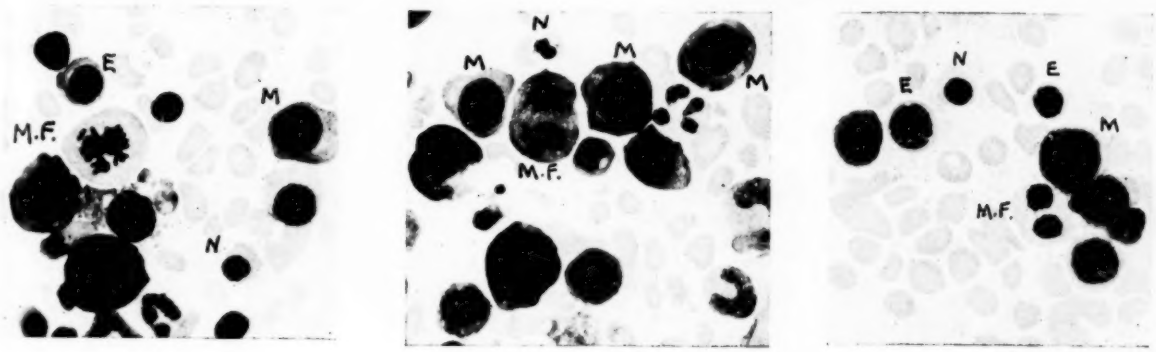

FIGURE I.
Photomicrographs of bone marrow films showing megaloblasts (M), erythroblasts (E), normoblasts (N) and mitotic figures in megaloblasts (M.F.). (×850.)

FIGURE IIA.
Photomicrograph of bone marrow film showing normal cellularity. (×100.)

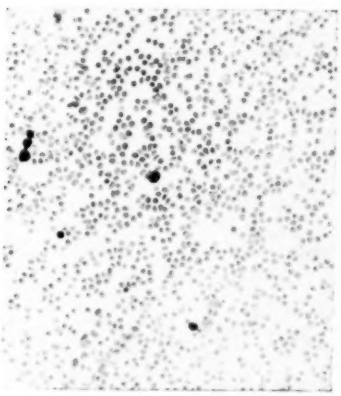

FIGURE IIB.
Photomicrograph of bone marrow film showing diminished cellularity. (×100.)

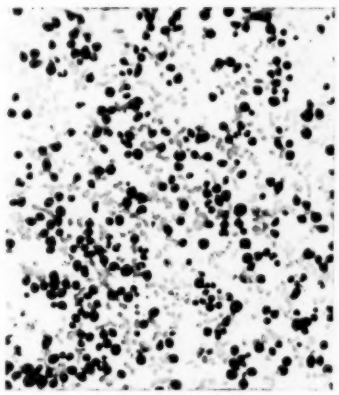

FIGURE IIC.
Photomicrograph of bone marrow film showing increased cellularity. (×100.)

FIGURE III.
Case XXVIII. Photograph of stomach showing ulceration.

FIGURE IV.
Case XXVIII. Photograph of duodenum showing ulceration.

FIGURE V.
Case XXVIII. Photograph of small intestine showing ulceration.

ILLUSTRATIONS TO THE ARTICLE BY Dr. R. A. WILLIS.

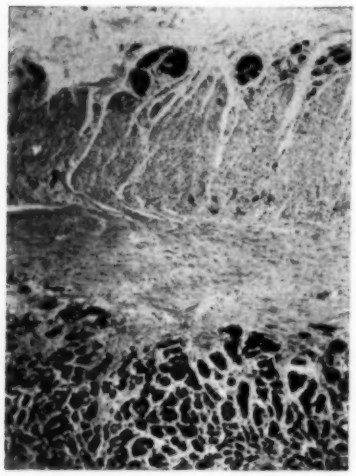

Figure I. (Case I).

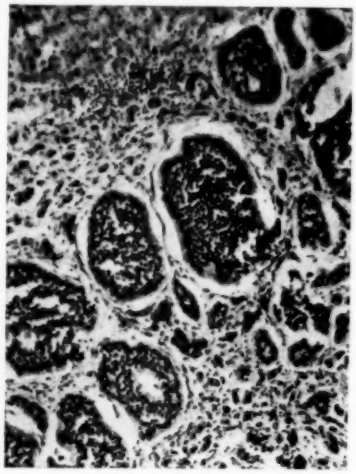

Figure II (Case III).

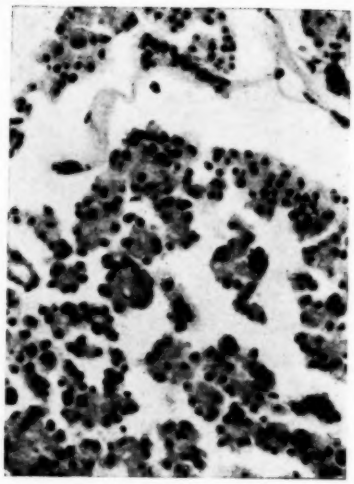

Figure III (Case IV).

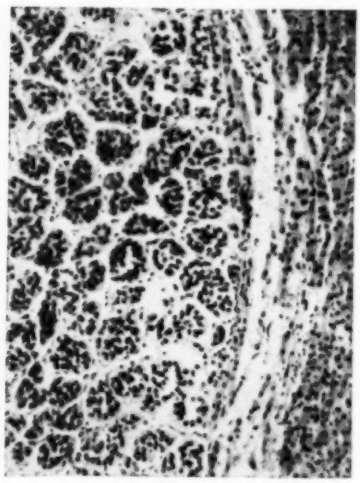

Figure IV (Case V).

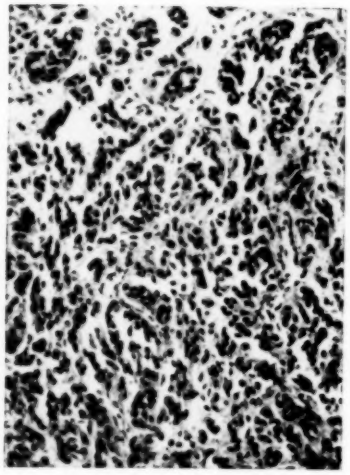

Figure V (Case V).

Figure VI (Case VI).

ILLUSTRATIONS TO THE ARTICLE BY Dr. HAROLD WILSON AND Dr. N. E. GOLDSWORTHY.

Figure I.

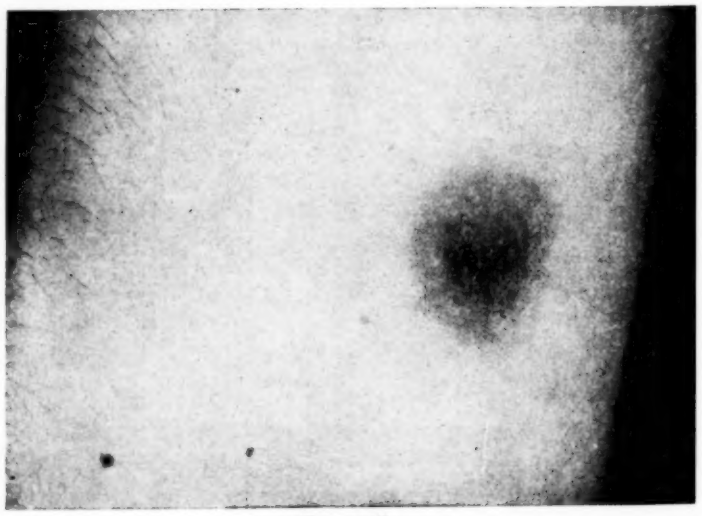

Figure II.

of coarse lobules by strong fibrous septa, so that if one succeeds in breaking down a few of these, how can one hope to influence the tension in the great number which are still intact? In the cases in which this treatment was used, there was no drainage from the tube, and I felt that the operative insult and the anæsthetic had merely intensified the metabolic *bouleversement* and that my well-meant but blundering efforts had but hastened the inevitable end.

That recovery is hindered rather than helped by operation is illustrated by the case of a Scottish golf "professional", whose clan slogan seemed to be "Down with whisky". This man was operated on in the approved style, and just got through with his life. In spite of warnings he remained true to his ideal, and, whether *post hoc* or *propter hoc*, he has had eight recurrences, mostly of equal severity to the first; but he has had little difficulty in dealing with them, though he was treated on expectant lines.

I understand from my medical colleagues that they do not now consider alcohol to be the deadly poison so many generations have held it to be; but one cannot escape the conviction that alcoholics get pancreatitis more often and more severely than the abstemious.

Again, if the patient gets over the hurdle of operation, severe post-operative distension is very common, so that the stitches cut out and allow the omentum or bowel, or both, to prolapse. This common complication, if not fatal, is almost invariably followed by a hernia.

The modern tendency, therefore, in acute cases diagnosed before operation is to rely on expectant treatment, as mentioned below; and if the condition is discovered only at operation, to close the abdomen and do precisely nothing except to suck out the beef-juice-like peritoneal fluid, for there is evidence that it contains active pancreatic enzymes. Our short, simple, Anglo-Saxon words are often deficient in the imagery and allusiveness of those derived from the more highly developed Romance roots, but they often make up for this apparent inferiority by their striking force; so if I may be permitted a word which gained great currency in the old Australian Imperial Force, I would say that it takes more "guts" to say "I have made a mistake and will do nothing more to harm my patient" than to embark on a face-saving operation of doubtful use and safety.

If conservative treatment is employed in these cases, in a good proportion the lesion will settle down entirely, while in a few it will reach the stage of a localized area of gangrene with a variable amount of inflammatory reaction. Now is the time for the judicious surgeon, for just as in pneumococcal peritonitis and streptococcal empyema, so in acute pancreatitis, watchful conservatism is becoming more and more popular, and operation is being reserved for the patient whose lesion has settled down and become localized.

Medical Treatment.

Medical treatment may be summarized as follows:

1. Absolute starvation is essential to put the pancreas at rest. The most that can be allowed is a minimum of water; but paraffin should be given liberally to combat the constipation.

2. Atropine should be given in full doses, because by depressing vagal activity it limits the production of ferments which, as I have mentioned earlier, are abundant in vagal juice.

3. In laboratory animals it has been shown that ephedrine diminishes pancreatic secretion for some thirty minutes after a latent period of ten to fifteen minutes. In the hope that this also occurs in man, doses up to 150 milligrammes every three or four hours have been given, apparently without obvious harm.

4. The duodenal tube is of great importance if much vomiting or distension is present. In order to be sure that the water balance is in the patient's favour, it is imperative to keep a balance sheet as advised by Dr. Ian Wood in *The Australian and New Zealand Journal of Surgery*, Volume VII, April, 1938, at page 340. Continuous siphonage as described by Wangensteen may be used, or the stomach may be aspirated and washed out at intervals of, say, two hours. It is likely that progressive estimations of the ferments in this juice may be of some use in prognosis, and will give helpful information when the time comes to resume the administration of food by mouth, for it is found generally that lipase first reappears, then trypsin, and amylase last; the fats should therefore be given first, then proteins, and carbohydrates last.

5. The continuous intravenous administration of saline solution should be begun as soon as it is seen that the fluid balance is against the patient, and the rate of flow depends on the profit or loss shown by this balance sheet. The manufacturing chemists have flooded us with a great deal of literature and other things; but they have done something really useful in providing such a wide range of solutions for intravenous use.

6. Glucose may be added to the saline solution if careful watch is kept on the urine, and if now and then the blood sugar content is estimated.

7. Insulin may also be indicated if the blood sugar level remains high, and if it is given with the necessary amount of glucose it may be used if acidosis occurs from the starvation.

8. Though the latest text-books on physiology suggest that blood transfusion is unsound unless hæmorrhage has occurred, I have seen it do so much good that I am satisfied to carry on till the physiologists again change their minds.

9. Finally, we must not let our new-found physiological zeal lure us into forgetting that we are dealing with a human being and not with a laboratory animal which will be sacrificed at the end of the experiment, and that human beings need rest. We must therefore make sure that we are not prodding the unfortunate patient with a hypodermic needle every hour or so. Morphine is one of God's gifts to sufferers and can be used freely, for research is tending to show that it does not inhibit peristalsis, as has been so long taught.

Surgical Treatment.

In subacute and chronic cases cholecystectomy is usually advised on the hypothesis that infection from the gall-bladder is the match which lights the fuse. It is known, however, that the subacute lesions often become chronic and that the chronic lesions are accompanied by fibrosis, which often leads to obstruction of the common duct. I would therefore suggest that to remove the gall-bladder is to remove an organ for which some unfortunate wight of a surgeon may one day sigh, so that by performing a cholecyst-gastrostomy he may make a by-pass round a block in the common duct.

This is quite a satisfactory operation, as instanced by the history of a florid full-blooded woman on whom I operated some seven years ago for gall-stones. Struck by the rubbery consistency of the head of the pancreas, I thought to myself that one day I might want that gall-bladder rather badly, and so performed a cholecyst-gastrostomy. The result has been excellent, her symptoms were quite relieved, and she lived to clear triumphantly some two years ago the hurdle of an abdomino-perineal resection of the rectum for carcinoma.

The appendix, that abdominal Ishmael, is a well-known murderer, and is rightly shot on sight. The uterus seems likely to share this unenviable proscription and, though innocent, to be not infrequently offered up as a victim on the altar of statistics. The radiologists have perfected the detective work of the cholecystogram and have the gall-bladder on the run, and I fear that the misguided enthusiasm of the hue and cry sometimes overwhelms judgement, for I feel that at least some gall-bladders are removed unnecessarily. Let us therefore make sure that the sins of the gall-bladder on which we are to pass judgement are really so heinous and the chances of reformation so small that it is obligatory to enforce the extreme penalty.

Some New Operations.

Pancreatic Adenomata.

An interesting development of pancreatic surgery has occurred as a result of the recognition of the causal relation of adenomata of the islet tissue of the pancreas

to attacks of hypoglycæmia. These growths, in common with similar tumours of the pituitary, thyreoid, parathyreoids, adrenals and ovaries, produce either an increase in the normal secretion or an abnormal secretion whose action is similar to that of the normal secretion. People who harbour these adenomata are thus always on the brink of a hypoglycæmic crisis, and when, as a result of diminished sugar intake or increased sugar destruction, the blood sugar falls below a critical level, symptoms of hyperinsulinism occur, and may vary from slight mental confusion and amnesia to coma, convulsions or manic attacks. Sweating, nausea, muscular langour and pallor may occur.

The Test for Hyperinsulinism.—Fraser and others have in *The Quarterly Journal of Medicine*, Volume VII, 1938, at page 115, described the application of the test for insulin sensitivity to the diagnosis of hyperinsulinism probably due to adenoma.

After twelve hours' starvation five units of insulin are given intravenously; the blood sugar content is estimated before the injection, and at thirty, sixty and one hundred and twenty minutes afterwards. If after the normal fall the blood sugar level does not return to normal in two hours, they conclude that hyperinsulinism is present, probably due to adenoma. The test, they state, is not dangerous so long as the patient is in good condition and the blood pressure is not low. It is advisable to stand by with readily administrable glucose in case the hypoglycæmia becomes dangerous.

Pathology of Adenomata of the Islet Tissue.—Adenomata of the islet tissue are usually benign and encapsulated, but they have been known to metastasize. They are often multiple and are more common in the tail and left half of the body of the pancreas than in the rest of the gland. Their colour is purplish, owing to the abundant blood supply, and they are firmer in consistency than normal gland tissue, so that careful palpation will reveal one which is not on the surface. It is stated that the predominant cell is the β-cell, the basophile granules of which are thought to be the precursors of insulin, and an extract of these tumours has been made which contains a high concentration of a substance that has the physiological action of insulin.

Operation.—The results of operation for removal of these tumours have been uniformly good in fifteen cases reported by Whipple—so much so that when in one case the glucose metabolism did not return to normal after one was removed, Whipple was confident enough to search for and remove another one with the happiest result. This reminds one of the confidence felt in searching for overlooked parathyreoid adenomata in cases of generalized *osteitis cystica*. The operation is performed through a wide transverse incision a little above the umbilicus, and, being rather formidable, would doubtless call for courage on the part of both patient and surgeon. This latter has not been lacking, for cases have been reported in which, after failure to find a suspected adenoma, the body and tail have been successfully resected; this is reminiscent of subtotal thyreoidectomy for thyreotoxicosis. One of the difficulties of this operation appears to be hæmorrhage from the pancreatic branches of the splenic artery, and one brave soul at least has tied this vessel and added a splenectomy to the already formidable subtotal pancreatectomy. Truly the race of giants is not extinct. Five of Whipple's patients were referred to him from a neurological institute to which they had been sent on account of peculiar behaviour and "queer turns". The possibility of this condition may well be kept in mind by psychiatrists and general practitioners, for the unfortunate people are sometimes unjustly accused of alcoholism and some have been thought to have epilepsy.

The story is told of a diabetic who felt an attack of hypoglycæmia coming, rushed into a restaurant, and in a highly peculiar manner called out "Sugar, sugar, sugar!" and was promptly thrown out; he as quickly returned, with the same result; but this time he grew so angry and made so much adrenaline that he mobilized enough glucose from his liver to tide him over the emergency, so that with a gesture of derision he picked up his hat and walked triumphantly off.

Carcinoma of the Head of the Pancreas.

Whipple has devised and with others carried out an operation for carcinoma of the head of the pancreas, a hitherto hopeless condition. The first stage is a cholecystgastrostomy and a posterior gastro-jejunostomy. Some weeks later the first and second parts of the duodenum and the head of the pancreas are removed. This is truly a *tour de force*; but Whipple has been rewarded by the survival of one patient for two years.

Illingworth has reported a very well-planned operation for this condition, by which one does not commit oneself irretrievably until it is reasonably certain that the growth is operable. He points out that this should be a carcinoma favourable to surgical treatment, as it is slow growing, metastasizes late, and often gives early warning by causing jaundice.

The first stage is the same as Whipple's. At the second stage the hepatic flexure is mobilized so that the duodenum and the head of the pancreas are exposed. The second part of the duodenum is then mobilized and swung forward and medially, so that it is possible to decide whether the growth can be separated from the inferior *vena cava*. If the superior mesenteric vein is then traced up to the groove it makes in the pancreas, a good idea can be formed as to the operability of the growth as far as the lower part of the portal vein is concerned; and this point can be cleared up for the upper part of the portal vein if the lateral edge of the gastro-hepatic omentum is incised and the portal vein is traced downwards, the common bile duct and the gastro-duodenal artery being tied at the same time.

By this time it can be decided whether the growth is operable or not, and yet the operation can if necessary be abandoned. If it is decided to go on, the pylorus is divided and invaginated, the junction of the second and third parts of the duodenum is divided and invaginated, the neck of the pancreas is then divided an inch to the left of the portal vein, and the pancreatic duct is ligated or sewn up. The head of the pancreas is then separated from the portal vein and inferior *vena cava* and the tissues between them.

This operation has been made possible by the recognition by Whipple that ligation of the pancreatic duct does not interfere with the secretion of insulin and that the loss of the external secretion can be made good by the *succus entericus*.

Conclusion.

Claude Bernard had a wife who thought a physiologist who made epoch-making discoveries was small beer alongside a successful and opulent doctor, which everybody said poor Claude could be if he tried. She therefore left him, and to sharpen the adder's tooth encouraged her daughter to become an active member of an anti-vivisection society and to lose no opportunity of harassing the sage. Truly he was worthy of some consolation. Among many other things he discovered the three pancreatic enzymes and the synthesis of glycogen, and coined the phrase "internal secretion". How it would have delighted his heart to know how neatly these intrepid surgeons have consummated his pioneer work on this, his favourite organ, by putting the coping stone on his brilliant researches!

Reports of Cases.

TWO CASES OF TRAUMATIC RUPTURE OF THE JEJUNUM WITHOUT PENETRATING WOUNDS OF THE ABDOMINAL WALL.

By ROBERT S. LAWSON,

Acting Surgeon to Out-Patients, Children's Hospital, Melbourne; Acting Surgeon to Out-Patients, Royal Melbourne Hospital, Melbourne.

CRUSHING INJURIES of the abdomen commonly result in the rupture of one of the solid viscera, and the signs of the accompanying hæmorrhage are important when the decision

to explore the abdomen has to be made. Exceptionally, rupture of the bowel may result from such an injury; and though it is well known that this can occur without a penetrating wound, its recognition may be delayed or intervention may be postponed in the absence of compelling signs of internal hæmorrhage. Needless to say, such delay is no less serious than in the case of rupture of a solid viscus. The following is an example of such a case.

Case I.

Clinical Record.

B.C., a boy, aged six years, was struck by a motor lorry at 1 p.m. on May 18, 1940. He was unconscious after the accident for a short time, and on regaining consciousness complained of abdominal pain. The child was admitted to the Children's Hospital at 3 p.m. He was conscious then, but was suffering considerably from shock and had a pulse rate of 140 per minute. There were numerous abrasions on the legs, on the right flank and behind the right ear; a large bruised area was present behind the right iliac crest, extending onto the buttock; and abrasions and bruising were noted in the anterior abdominal wall in the lower and middle zones. No fractures of ribs or other bones appeared to have been sustained, while examination of the thorax indicated no special injury in that region. The abdomen was rigid and tender, especially in its lower half, but without any abnormalities of dulness or tympany to percussion. The pupils and reflexes were normal.

After his admission to hospital the child vomited; but the vomitus contained no blood. Urine was obtained by means of a catheter, and it was clear. Rectal examination revealed no abnormality. Under observation the child lay quietly in bed and made no special complaints, though he agreed on questioning that his "tummy was still sore". The pulse improved, and at 7 p.m. its rate had dropped to 120 per minute, with increased volume. The shock had abated somewhat and the colour in the cheeks was good. However, the abdominal tenderness and rigidity were no less pronounced, and although it was realized that this could well be due to the obvious bruising of the abdominal wall, it was decided to explore the abdomen. The possibility of a ruptured bowel could not be eliminated, and it was felt, therefore, that further delay would be indefensible. It should be mentioned that the young pedestrian declared that the motor lorry ran right over him; but in the absence of other witnesses this statement was regarded with scepticism.

Operation was performed at 7.30 p.m. under ether anæsthesia. The abdomen was opened by a right lower paramedian incision and the peritoneal cavity was found to be soiled with a little discolored fluid and flecks of mucous material. The caecum was found to be intact, and likewise the colon as far as could be ascertained. The small bowel was then traced up from the ileo-caecal junction, and in the upper portion of the jejunum, about eighteen inches from the duodeno-jejunal flexure, the rupture was found; it was a transverse tear across three-quarters of the circumference of the bowel, while the mesenteric attachment was intact. This tear was repaired by suture; but the remaining lumen was so reduced in size that it was decided to perform side-to-side anastomosis as well. Accordingly this was done between those portions of bowel immediately above and below the sutured rent. The abdomen was then closed without drainage. Convalescence was uneventful. X-ray films taken during this period revealed green-stick fractures of both rami of the pubis on the left side and a vertical fissure in the fourth segment of the sacrum. There was no fracture in the lumbar portion of the spine. After his discharge from hospital on June 4 the child was kept in bed for six weeks at the after-care home. Seen in the out-patient department on July 18, he appeared perfectly well. The fractures had united, and he seemed none the worse for his experience.

Discussion.

The only plausible explanation of this lesion would seem to be that the child was quite right—that is to say that the motor lorry did run right over his abdomen and that the jejunal loop was nipped between the lorry wheel and the vertebral column. The lumbar portion of the spine, however, received no bony injury, and one must assume that it escaped fracture owing to its youthful resilience. In this regard it may be instructive to recall that merely to run over a snake with a motor car is not sufficient to break its back. Readers of the "Aboriginalities" column in *The Bulletin* know that to effect a kill, the brake must be applied as the wheel passes over the reptile.

Case II.

The second case reported here emphasizes again the fact that abdominal tenderness and rigidity are imperative reasons for exploring the abdomen after trauma, even in the absence of a penetrating wound or of any other positive sign of internal injury.

Clinical Record.

R.W., a male, aged twenty-two years, was thrown off his motor cycle at 5.30 p.m. on June 12, 1940, after he had collided with a motor car. He was admitted to the Royal Melbourne Hospital with a fractured left femur in the lower third of the shaft, a comminuted fracture of the left tibia with the wound of a small compound fracture in the middle of the leg, and a crushed left foot with fractured metatarsal bones, also complicated by the wound of a small compound fracture. When seen at 8 p.m. he was suffering severely from shock; his pulse rate was 140 per minute, and his systolic blood pressure was 86 millimetres of mercury. The limb had been placed temporarily on a back splint and antiseptic dressings had been applied to the wound; the pain had been relieved somewhat by the administration of morphine. The patient complained, however, of a pain in the lower part of his abdomen, "as if he wanted to pass water". A catheter was passed without difficulty and clear urine was drawn off, but the pain persisted. Examination of the abdomen revealed no evidence of external injury whatever, but tenderness and some slight rigidity were noted in the left lower abdominal quadrant. In reply to direct questioning the patient stated that the handle of his motor cycle might have struck him there, but no bruising was to be seen. It was thought possible that internal injury had been sustained; but as the patient was suffering so severely from shock, some hesitation was felt in opening the abdomen without a reasonable certainty of finding something to justify the procedure, and it was decided to await developments for a couple of hours.

At 10 p.m. the signs were substantially unchanged. The pulse rate was 130 per minute and the systolic blood pressure was 96 millimetres of mercury. No local signs of hæmorrhage into the abdominal cavity or of the presence of free gas were elicited. There was no shoulder pain. The sole indication for exploration of the abdomen was the persistent tenderness and rigidity in the left lower abdominal quadrant. Laparotomy was decided upon.

At 10.30 p.m., under ether anæsthesia, the abdomen was opened by a left lower paramedian incision. The peritoneum was found to be soiled with a little brownish fluid and flecks of half-digested food. As the sigmoid colon appeared intact, the duodeno-jejunal flexure was sought for, and about ten inches below it a transverse rupture of the bowel on its antemesenteric border was found, about one inch in length. Material leaking from this rent had drained down between the descending colon and the spine; this accounted for the localization of the abdominal signs to the left lower quadrant. The bowel was repaired with two layers of sutures and the abdomen was closed without drainage. The fractures of the lower limb were then rapidly dealt with by traction from a Kirschner wire through the *os calcis*, the limb being placed on a Thomas's splint. The small compound wounds were excised, douched with flavine solution and sutured. Antitetanic serum was given and the patient was returned to bed. He was then suffering severely from shock and his pulse rate was 160 per minute. Saline solution was given intravenously, and various stimulants *et cetera* were administered. Twelve hours later the patient's condition gave rise to some hope, the pulse rate having dropped to 120 per minute; but on the following night he lapsed and he died at 4 a.m. the next day—that is, about thirty-six hours after the accident. Though he was of strong constitution, the severity and multiplicity of his injuries was more than he could withstand.

Discussion.

In this case it seems probable that the rupture of the bowel occurred in a way similar to that in the first case reported—that is, by crushing of the bowel against the vertebral column. The handle of the motor cycle projecting swiftly into the unguarded abdominal wall was no doubt responsible.

HIGH BLOOD UREA LEVEL, OLIGURIA AND EXTENSIVE SKIN REACTION FOLLOWING THE INGESTION OF SIX TABLETS OF "M & B 693".

By Donald Finlay, M.B.,
Sydney.

On July 11, 1940, I was called to see Mr. V.R., aged sixty years, merchant. He was suffering from severe pharyngo-tracheitis. His temperature was 100·5° F., and his

pulse rate was 80 per minute; his systolic blood pressure was 140 millimetres of mercury and his diastolic blood pressure 80. He had had no illness in the past eleven years.

The usual symptomatic treatment was prescribed. On July 13 his temperature was 101·5° F., and a few râles were detected at the base of his right lung. The nurse was told to give him three tablets of "M & B 693" that evening and two tablets every four hours according to instructions. Three tablets were given at 6 p.m. and two at 10 p.m. He slept through the night. As he was slightly nauseated in the morning, one tablet only was given at 8 a.m. He still felt nauseated. His temperature was down to normal, so I instructed the nurse to discontinue the administration of the tablets.

On the evening of July 14 he complained of a slight irritation of the skin. On July 15 a widespread general rash was present. On July 16 he passed 25 ounces of urine, the irritation of his skin was extremely severe, and there were angio-neurotic swellings on the side of his face and on the dorsum of one foot. On this day I saw him in consultation with Sir Charles Blackburn, and it was considered that in view of his restless, somewhat disorientated, state, his renal function might be disturbed in spite of the absence of change in the urine. Sir Charles doubted whether the small amount of "M & B 693" taken could be incriminated, especially as there was no evidence of renal inflammation; but he later telephoned to me to say that on looking through the literature he had found records of two cases in which, after the administration of comparatively small amounts of "M & B 693", there had been diminished urinary output with high blood urea level, but no hæmaturia such as is usually recorded when crystals are deposited in the tubules.

On July 17 the patient passed 35 ounces of urine, and on July 18 he passed 20 ounces. His temperature was only slightly elevated. On July 19 a blood count was made and the following information was given: The red cells were regular in size and shape and full of hæmoglobin; the white cells were all mature and the platelets were plentiful. Dr. Marjorie Little reported that the urea content of the blood was 210 milligrammes per 100 cubic centimetres. The specimen of urine gave an alkaline reaction; it contained a faint trace of albumin and its specific gravity was 1,022; the urea content was 2·2%, and it contained no cells and an occasional hyaline cast.

When this report was received the patient was encouraged to drink freely and was given potassium citrate in large doses. As the angio-neurosis was found to be relieved by adrenaline, this was given by hypodermic injections; five mils of a 1 in 1,000 solution were given three times a day.

On July 19 the patient was seen by Dr. E. H. Molesworth, who reported as follows:

> There is now a widespread rash involving nearly all the body surface, erythematous and follicular in nature. It is worse in the flexures and in the seborrhœic areas, retro-auricular, naso-labial, umbilical *et cetera*. On the lower parts of the legs the rash is purpuric. The hæmorrhages are numerous but individually small, rarely exceeding 1/2 centimetre in diameter.

A lotion was prescribed containing calamine, zinc oxide, rectified spirits of wine, glycerin and lime water. Morphine was necessary to enable the patient to rest at night.

On July 20 the patient passed 110 ounces of urine, on July 21 he passed 88 ounces, and on July 22, 80 ounces. The rash was still troublesome; but on July 23 the urea content of the blood was 40 milligrammes per 100 cubic centimetres of blood. The urine gave an alkaline reaction, and it contained no albumin, no cells, no casts and no crystals.

In the following week the patient had three mild recurrences of the rash, once after partaking of some stout and twice after taking "Liquor Somnos" at night for sleep. Stout and "Liquor Somnos" were accordingly forbidden, and Vichy and Carlsbad waters were prescribed; of these (*mirabile dictu*) the patient appeared to possess unlimited quantities. There have been no further symptoms, and convalescence has been uninterrupted.

Reviews.

PHYSIOLOGICAL CHEMISTRY.

For twenty-five years Mathews's "Physiological Chemistry" has been a standard text-book; it now appears in its sixth edition. This well-known work retains on the whole its original form, except that the practical portion has been omitted; this modification is wise. The subject of biological chemistry has now grown to such an extent that attempts to include practical sections in theoretical text-books, while retaining reasonable dimensions, often result in unsatisfactory compromises. The theoretical portion of the first edition occupied some 850 pages. The present edition has some 1,500 pages.[1]

The first part of the book has chapters on the general properties of living matter and the physical chemistry of protoplasm, and deals with the chemistry of lipides and proteins on conventional lines. Carbohydrates are dealt with much more fully and rather differently. The author has strong convictions as to the importance of the part played by carbohydrates in living tissues. He has been led to include in this part discussions of glycolysis, of the metabolism of muscle, and of newgrowths, which might more logically have been dealt with in the chapters treating of metabolism. Even the nucleic acids are considered here as carbohydrate derivatives. Although the author's views are somewhat extreme, his discussion of the carbohydrates is a very valuable part of the book.

Apart from a lack of balance, about which there may well be difference of opinion, this part of the book has some serious defects. One might, for example, have expected a discussion of the mineral constituents of the body; but this is relegated to the last chapter of the book, where it follows that on vitamins. This is another instance of the tendency of biochemists, in their preoccupation with the quantitatively predominating organic constituents of the cell, to lose sight of the fundamental importance of the mineral constituents of the medium in which the cell carries on its activities. It is a survival of the attitude of mind which prevailed during one phase in the history of biochemistry. Towards the end of last century it seemed that it might be possible to explain the chemical activities of the living body in terms of reactions of carbohydrates, fats and proteins. There was a tendency to regard the minor constituents, which did not fit into these groups, as impurities and to lump them together for discussion, usually at the end of the book. These minor constituents no longer demand attention solely because of their nuisance value. Their importance is well established. Indeed, these formerly repressed minorities of the biochemical world may at the moment be receiving a little more attention than is their due.

This portion of the book also includes a small and inadequate discussion of enzyme action. It is true that the action of the more important individual digestive enzymes is discussed in some detail in the appropriate chapters, but a fuller general discussion would have been useful. The essential part played by enzymes in most of the chemical reactions of the body cannot be denied, even if one is not prepared to go all the way with the authors of a recent German text-book, when they assert boldly that all progress in biological chemistry has been due to the study of enzyme action.

There are also some astonishing omissions from the chapter on proteins. One of the most striking advances in this field has been due to the work of Svedberg and his school at Upsala. By means of the ultracentrifuge, which has now been developed to a high degree of efficiency, this investigator has been able to obtain data on the weight of the protein molecule by a method singularly free from objections such as can be raised against most other methods. Yet this outstanding advance receives no mention beyond a brief paragraph giving some of the results obtained.

Another recent event of considerable importance in the same field is the development by Dr. Dorothy Wrinch of the cyclol hypothesis of the structure of the protein molecule. Although some details of this hypothesis still lack experimental support, it gives such a clear, coherent and logical representation of certain classes of these huge molecules that its appearance must be regarded as an event of major significance in the development of protein chemistry. But this hypothesis does not appear even to be mentioned.

The rest of the book deals with nutrition in the broad sense of the term, and with the composition of the more important tissues of the body. It is in this part of the book that one sees the old Mathews. The body as a whole is discussed as a biochemical mechanism in the attempt to correlate its varied activities, although one very important aspect of these activities, oxidation-reduction processes occurring in the tissues, receives inadequate treatment.

In this part of the book too one finds a store of information much of which is difficult to find elsewhere. The more experienced biochemist will value this book also for the intentionally provocative manner in which the author presents some of his views. The book is, however, hardly suitable for the medical student or for the reader not already fairly conversant with the subject.

[1] "Physiological Chemistry: A Text-Book for Students", by A. P. Mathews, Ph.D.; Sixth Edition; 1939. London: Baillière, Tindall and Cox. Medium 8vo, pp. 1504, with illustrations. Price: 44s. net.

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THE BARBITURATE PROBLEM.

THE hurry and pressure of life and the noise that goes with it make great demands on the nervous system of man; few people saunter through life as we are led to think they did a generation or two ago. Even if people of a past age did have to face wars, riots or turmoil, they were not all forced to take part and many were able to be in leisure or to live workaday lives unmoved by passing events. That many people today cannot withstand the stress of life need cause no surprise. It is, of course, true that were men and women the product of a race inured to hardship and trained to withstand stress of body and mind, neurosis might not be so prevalent and nervous breakdown so common as it is. Man in distress often needs a prop on which to lean, and to such a one the barbiturates are a tremendous boon. Properly used, they will tide a harassed person over a period of stress and restore to health many who have faltered. But their use is fraught with danger because of the ease with which they induce sleep or preserve a natural peace of mind. Barbituric drugs are at once easy to take, beneficent and dangerous—and here lies the problem. The problem is not obscure, as are so many problems in medicine that have to do with a disease whose pathogenesis is unknown; here we are dealing with drugs known to act in a certain way, known to be most useful and known to be both dangerous and abused.

A discussion on barbiturates is made easier if we remember the classification of Tatum and Fitch, in which they divided depressant barbiturates according to their period of action—long, intermediate, short and ultra-short. (See THE MEDICAL JOURNAL OF AUSTRALIA, February 10, 1940, page 198.) Barbital and phenobarbital belong to the long-acting group; "Neonal" and "Dial" are intermediate actors; "Amytal" and "Nembutal" are short actors; and "Evipal" and "Pentothal" are ultra-short-acting barbiturates. Under certain conditions, as when the liver is inactive or has been injured, short-acting drugs may behave as long actors and cumulative effects may occur. Barbitone or veronal (diethyl barbituric acid) is the simplest member of the group, and the toxicity of the substance is increased by the addition of alkyl or aryl radicals of higher molecular weight than ethyl. Of the value of barbiturates there can be no doubt. The clinical indications for their use have been grouped under five headings: hypnotic, pre-anæsthetic depressant, anæsthetic, anticonvulsant and neuro-psychiatrical. The temptation to discuss these indications must be resisted; but it may be stated that there is every justification for the view that, when they are properly given, the barbiturates are the most useful of all sedatives; and it is well to recall that by taking them, even for long periods, many men retain their mental activity late in life. At the same time too much emphasis cannot be laid on the fact that these drugs are not analgesic. A barbituric acid compound has sometimes been combined with an analgesic drug, such as amidopyrine or phenacetin, and when this is done caution is more than ever necessary. The combination is effective in many conditions and is freely used, but many prominent clinicians regard it as dangerous. They point out that the barbituric drug is much more toxic than the analgesic, and that overdosage may easily occur. Useful conclusions were drawn by C. P. Wagner, writing in *The Journal of the American Medical Association* on December 2, 1933, on the pharmacology of the barbiturates. He stated that though they were usually employed for their sedative action, the barbiturates influenced almost every system of the body, and that their side actions should be considered in relation to the general condition of the patient. He pointed out that the longer acting drugs were eliminated slowly and that the cumulative effect of long-continued usage might lead to a delirious reaction or to other toxic symptoms. The psychological reactions, readily induced by the drugs acting over a shorter period, usually helped in gaining cooperation from the patient, and might interrupt the course of a psychosis and hasten recovery. Wagner also expressed the opinion that if the drug was given over a long period the histological changes produced by the administration of large doses might lead to permanent impairment of function. In regard to this last-mentioned opinion, it must be remembered that degenerative changes have been found in the nerve cells of animals to which barbituric acid compounds have been given over long periods.

When the results of the careless use of the barbiturates are considered mention must first of all be made of the idiosyncrasy shown by some people—symptoms of acute poisoning have followed what is regarded as a normal full dose, and Willcox has recorded the occurrence of coma, suppression of urine and bronchopneumonia following a dose of three grains of "Nembutal" taken by mouth. Idiosyncrasy, however, must be extremely rare; carelessness is generally the cause of untoward happenings, and not infrequently these drugs are used with suicidal intent. In this regard attention may be directed to a report that has been drawn up at the instance of the Council on Pharmacy and Chemistry of the American Medical Association. The first part of this report was issued in *The Journal of the American Medical Association* of April 8, 1939, under the title of "The Promiscuous Use of the Barbiturates" and had to do with their use in suicides; the second part has appeared in the May 18,

1940, issue of the same journal. The report is from the pen of W. E. Hambourger, of the department of pharmacology of the Western Reserve University school of medicine. Hambourger stated in the first part of his report that during 1936 more than 1,200,000,000 grains of barbituric acid were sold in the United States of America. The number of suicidal deaths by the barbiturates in 1936 was close on 300; in 1937 they probably exceeded 400. The incidence of suicides by barbiturates was nearly twice as high in large cities as in the country as a whole. The second part of the report, which is an analysis of hospital data, shows that during the decade 1928-1937 thirteen hospitals with a combined admission total of more than 1,250,000 received 643 patients suffering from acute barbiturate poisoning, or 1 in 1,900. The fatality rate among the 643 patients was 7·3%. The lowest fatal dose of barbital was thirty grains; the medium dose in fatal cases was ninety grains. For phenobarbital the lowest fatal dose was twenty-five grains and the medium fatal dose 142 grains. The wider margin of toxicity for phenobarbital was looked on as probably accidental. It is interesting to note that thirteen patients admitted to ten hospitals were thought to be hypersusceptible to the drug. One of the most important statements in Hambourger's report is that as each new barbiturate was introduced clinically and became "publicized" there was a notable trend towards its use as a poison. Hambourger has something to say about addiction to barbiturates and the number of persons in whom this phenomenon was noted. Before reference is made to his statements it may be well to ask whether the word addiction can ever be applied to the constant use of barbituric drugs. Addiction has been aptly described by Tatum and Seevers as "a condition developed through the effects of repeated actions of a drug such that its use becomes necessary and cessation of its action causes mental or physical disturbances". Most clinicians will subscribe to this definition. In an article in *Physiological Reviews* published last October, Tatum insisted that repeated and continued use of barbiturates induced a condition of habituation or psychic dependence, but not a true addiction as exemplified by the use of morphine. He points out that mental disturbances occur during the period of drug taking, and adds that they are obviously due to the positive action of the drugs rather than to the cessation of drug taking or abstinence phenomena. At the same time Tatum admits that Schmidt described what appeared to be withdrawal symptoms, and he also refers to the contentions of such writers as Weiss and Robinson that irreparable damage may possibly occur in the brain and other tissue cells as a result of abuse of these drugs. Such damage, as already mentioned, has been described as occurring in the dog after the administration of large doses of barbiturates. From clinical experience and from the other available evidence it is probably wise to conclude that the condition arising in man after the prolonged use of barbiturates is an habituation and not a true addiction. Turning once more to Hambourger's report, we find that what he calls addiction to barbiturates was the reason for the admission to hospital of 85 of the 643 patients, and two-thirds of these claimed that they had become familiar with the drug through a medical practitioner. Nearly one-third of the "addicts" in regard to whom the information was recorded developed craving when the drug was withheld, but (a point to be emphasized) none manifested any withdrawal symptoms.

Part of the story of the barbiturates has been told—reference has been made to their great value and to the way in which they may be abused, and this is the most important part of the story. The practical point that arises has to do with the precautions necessary to their use in medical practice. Generally speaking, it is advisable that patients should not know what drug they are taking; and with this object in view, though not likely to be entirely successful, proprietary preparations should not be dispensed in their original containers. Some patients may be warned of the danger of taking more than the prescribed dose; sometimes the warning may be given to the patient's relatives or responsible friends. The friends may be made aware of the peculiar condition known as automatism. In this condition the patient, having become accustomed to the use of drugs, may some time or other find that sleep will fail him with his usual dose; he is partly under the influence of the drug, in what has been called the twilight zone, and, not being able to exert normal inhibition or reason, takes all the remaining doses that he has. Death in these circumstances is unintentional or accidental; but this point is outside the present discussion. Fortunately patients cannot obtain barbituric drugs without a prescription from a medical practitioner; and we must presume that all practitioners are thoroughly familiar with the indications for their use and will observe them with the greatest care.

Current Comment.

SULPHAPYRIDINE THERAPY IN PNEUMONIA.

ALTHOUGH three months have not yet elapsed since the publication in this journal of the articles by Dr. A. W. Holmes à Court and Dr. A. G. Cumpston on sulphapyridine treatment in pneumonia, and by Dr. Alex. Murphy on the clinical application and toxic effects of sulphanilamide and sulphapyridine, reference must be made again to the use of sulphapyridine in pneumonia because of two interesting studies that have recently appeared. H. K. Detweiler, H. I. Kinsey, W. Hurst Brown and W. R. Feasby have written from Toronto, Canada, on toxic reactions during the treatment of pneumonia with sulphapyridine,[1] and K. G. Kohlstaedt and I. H. Page on the treatment of pneumococcal pneumonia with sulphapyridine.[2]

There should be no need at this stage to recall the great reduction in mortality that has followed the introduction of sulphanilamide compounds, particularly sulphapyridine, in the treatment of pneumonia; but it may be well to keep it in mind when the toxic effects of these drugs are considered. (For a discussion on the particular virtues of sulphapyridine over other sulphanilamide drugs in the treatment of pneumonia readers are referred to the recent article in this journal by Dr. Alex. Murphy.) All comparative figures of deaths from pneumonia before and after the introduction of sulphapyridine, given by both Detweiler and Kohlstaedt, may therefore be omitted.

The patients reported by Detweiler and his co-workers are divided into two groups. In the first are included 18 suffering from pneumococcal pneumonia who received a dosage smaller than that received by the 70 patients who comprised the second group. It was among those in the second group that the toxic manifestations chiefly became

[1] *Archives of Internal Medicine*, June, 1940.
[2] *Annals of Internal Medicine*, July, 1940.

evident. The first group of patients received an initial dose of two grammes of sulphapyridine, and this was followed in two hours by another two grammes; then one gramme was given every four hours for six doses; on subsequent days the four-hourly dose was reduced to 0·5 gramme. The average total dose received by these patients was 22 grammes. The second group were given two grammes every four hours for six doses, then 1·5 grammes for six doses, then one gramme for six doses, and finally 0·5 gramme for six or more doses. The average total dose received by these patients was 35 grammes. The dosage given by Kohlstaedt and Page is described as follows. The total amount of sulphapyridine given varied from patient to patient, but the dose during the first thirty-six hours was standardized. Treatment was begun with an initial dose of two grammes, followed by one gramme at two or three hour intervals during the next thirty-six hours. This approximated a total dose of one grain per pound or 0·12 gramme per kilogram during this period. Further administration depended on (*a*) the severity of the toxic manifestations, (*b*) the rectal temperature at the end of thirty-six hours, (*c*) the concentration of free sulphapyridine in the blood, (*d*) the change in the number of leucocytes. It will be remembered that in the Sydney Hospital series reported by Cumpston one gramme of sulphapyridine was given every four hours day and night until the temperature had been normal for forty-eight hours; then one gramme was given every six hours for a further twenty-four hours. In this way the majority of patients received between 20 and 30 grammes of sulphapyridine.

The effectiveness of sulphanilamide compounds depends, so it is generally understood, on the concentration of the drug in the blood. Detweiler and his collaborators believe that no definite statement can yet be made regarding the optimum concentration of sulphapyridine in the blood; they have had as a goal, however, an initial level of six milligrammes per hundred cubic centimetres and a maintenance level of four milligrammes. In Cumpston's series, 36 of 63 patients had a uniform sulphapyridine level of over four milligrammes *per centum* during the period when the drug was given every four hours. In the other 27 cases the level varied; in 11 cases the reading was over four milligrammes, and in 16 it was under this level. Cumpston found that no correlation could be obtained between the concentration of sulphapyridine in the blood and the temperature response or the occurrence of delayed resolution. Kohlstaedt and Page, as already stated, used the concentration of free sulphapyridine in the blood as one of the indications for continued administration of the drug. They were unable to establish a direct relationship between dosage and free sulphapyridine in the blood; on several occasions large doses failed to raise the blood level to the high concentrations observed in other patients who received smaller amounts of the drug. They also make the important observation that a high concentration of the drug does not ensure recovery, for in their four fatal cases the maximum concentrations were respectively 18, 14 and 11 milligrammes per hundred cubic centimetres. The explanation of these important observations is not simple. To begin with, the infecting organism may be presumed to present varying degrees of virulence; again, it may be so securely entrenched or peculiarly situated that it is safe from even high concentrations of the drug; again, in view of the recent work of Fildes and of Woods, mentioned in these columns in the issue of September 28, 1940, it is not inappropriate to wonder whether some obscure chemical reason may not be responsible.

In the matter of toxic manifestations these reports are instructive. Detweiler and his co-workers found that with his earlier and lower dosage practically no toxic symptoms were noted. It was with the higher dosage, totalling on an average 35 grammes, that serious toxic manifestations occurred. Most of their patients experienced nausea and vomiting; in about 10% the vomiting became a serious obstacle to treatment. Vomiting and nausea were the only serious complications during treatment noted by Kohlstaedt and Page; they "became important" in about a quarter of them. Vomiting was present in 50% of Cumpston's cases, but was rarely severe enough to necessitate suspension of the drug. The relief of nausea and vomiting is difficult. Cumpston found that partial relief was obtained if the drug was given in powdered form in milk or fruit juices; Detweiler found this method ineffective. Both observers found that nicotinic acid gave relief. Detweiler and his collaborators gained results from the administration of 100 to 300 milligrammes of nicotinic acid in every twenty-four hours. Cumpston gave 50 milligrammes of nicotinic acid with each dose of sulphapyridine. Detweiler and his co-workers have also had success by giving the sulphapyridine in the form of an emulsion and adding the nicotinic acid to it. Another method that has been tried in order to obviate nausea and vomiting is administration of the drug by the parenteral route. Detweiler and his fellow workers find that even when the intravenous route is used nausea and vomiting still sometimes occur; they think, therefore, that the vomiting may have its origin in the central nervous system. Though their experience of the method has been "limited", they express the view that it should be used only when the drug cannot be given by mouth. It is interesting in this connexion to recall that Gaisford, Evans and Whitelaw, writing in *The Lancet* in July, 1939, claimed that the intramuscular injection of "M & B 693" was less liable to cause reaction and vomiting than when it was given in any other way.

Apart from nausea and vomiting, the less serious toxic manifestations of sulphapyridine therapy are anorexia, headache, twitching of the face, and cyanosis. Cyanosis may be due to the presence of sulphæmoglobinæmia. The "serious" toxic manifestations listed by Detweiler and his co-workers are: oliguria, anuria, gross hæmaturia, leucopenia, anæmia, cutaneous rashes, thermal reactions and mental changes. These they considered to be indications for the partial or complete withdrawal of the drug. The toxic manifestations encountered by Kohlstaedt and Page included occasional leucopenia, rare anæmia and hæmaturia. These will not be discussed on this occasion. It is important to note that the more severe toxic manifestations described by Detweiler and his co-workers occurred with their higher dosages. We may leave the subject for the present by accepting their statement that heavy doses should be employed with great caution. At the same time we must realize that the subject is vast and that much yet remains to be clarified.

DERMATITIS FROM RESINOUS FABRIC-FINISHING MATERIALS.

A study has recently been made by Louis Schwartz, Medical Director of the United States Public Health Service, and seven other authors, of an outbreak of dermatitis that occurred in Canada and the United States from the use of a new resin material employed in the finishing of fabrics.[1] In some instances the dermatitis was severe and systemic symptoms occurred, making admission to hospital necessary. The substance found to be responsible was an acid ester gum, of which the finishing material was an emulsion. The outbreaks of dermatitis occurred in several centres, but were all traced to a common cause. The view is expressed that manufacturers of wearing apparel containing new chemicals should have studies made of the effect of these chemicals on the human skin before the clothing is sold to the public. The chemical, it is held, should first be tested on susceptible animals to determine whether it is a primary skin irritant; if it is not, its sensitizing properties should be tested on animals by means of a patch test. Wearing apparel containing chemicals which have not been used before on fabrics, should be tested on ten or twelve persons to determine whether it acts as a primary skin irritant or sensitizer. If it does not affect these people, a larger number of persons (200) should be tested by a patch test for five days; a control test should be used. In any case, all new underwear should be washed before it is worn.

[1] *The Journal of the American Medical Association*, September 14, 1940.

Abstracts from Medical Literature.

THERAPEUTICS.

The Prescription of Aspirin.

In an annotation in *The Lancet* of February 10, 1940, it is noted that acetylsalicylic acid decomposes into the gastric irritant salicylic acid quite slowly when in suspension—at the rate of 7% or 8% a month; solutions with potassium citrate or ammonium acetate decompose much more rapidly. A good prescription is: *Acidi Acetylsalicylici*, 80 grains; *Pulvis Tragacanthæ Compositi*, 40 grains; *Syrupi Limonis*, one fluid drachm; *Aquam Chloroformi*, to eight ounces. Half an ounce of the mixture is taken as occasion arises.

Aluminium Hydroxide Gel in Peptic Ulcer.

E. S. Emery and R. B. Rutherford (*The New England Journal of Medicine*, February 8, 1940) present their results of the later course of treatment of twenty-eight patients concerning whom a previous communication was made. The following are the advantages of aluminium hydroxide gel over other forms of alkali therapy: slight absorption, fair neutralizing capacity and astringent action tending to decrease secretion of acid. In mild cases any form of alkali therapy will evoke a response, so only severe cases have been selected for observation. Fourteen of these patients were followed for eleven to eighteen months, and eight have had no further symptoms and can be regarded as well; two are classed as satisfactory, having had a return of mild symptoms on one or two occasions. The remaining four are unsatisfactory. It is interesting to note the high percentage of well patients in a group chosen for the severity of the disease. All but three of the series would have been recommended for surgical intervention if they had not been made the subjects of investigation in the use of aluminium hydroxide gel. The use of this line of therapy is only another way of neutralizing gastric acidity, and it does not hold out any greater hope of ultimate cure than do the other methods of antacid treatment; but it is the opinion of the authors that in aluminium hydroxide gel they have found the most effective drug for the control of severe cases during the period of acute activity. It now appears that if special attention is given to these patients many of them can be carried along satisfactorily on a medical régime provided they are willing to take five or six doses of the gel a day. It is concluded that in severe cases trial should be made with the gel before subtotal gastrectomy is advised.

Citrated Plasma in Secondary Shock.

Max M. Strumia *et alii* (*The Journal of the American Medical Association*, April 6, 1940) draws attention to the advantages of using citrated blood plasma instead of the transfusion of whole blood. The treatment of shock demands a rapid and permanent increase in the patient's blood volume; there are two essential drawbacks to the use of whole blood, namely, the interval of time necessary to prepare the transfusion and the undesirable addition of red cells to the already concentrated blood. The employment of preserved citrated blood promised to overcome the first of these objections; but there are still difficulties in this procedure—the limited period of usefulness of such blood, the undesirability of transport causing mechanical agitation and breakdown of erythrocytes, and the time needed for direct compatibility tests. Plasma has the advantage over saline, glucose and acacia solution of having a high protein content giving a high colloidal osmotic pressure, and is readily obtained by centrifugation of citrated blood either immediately or on expiration of the useful period of preservation in the blood bank. Further advantages are: its readiness for immediate use without typing and compatibility tests, the fact that large and repeated doses can be given at any interval of time without untoward effect, the failure to add to the concentration of erythrocytes, and ease of transportation and preservation. At 4° C. the protein content of plasma, and therefore its anti-shock properties, can be preserved for months; in the frozen state it can be preserved for an even longer period. Finally, reduced to a dry powder by desiccation, it can be kept for an indefinite period and readily prepared for use by regeneration with distilled water. The average dose is about 500 cubic centimetres; but this varies. It is advised that the dosage be adequate to relieve entirely the symptoms of shock. It is usually administered at the rate of 10 cubic centimetres per minute. It can be diluted with an equal quantity of saline and dextrose solution. Heating of the plasma must be carefully avoided; the administration of cold plasma causes no reaction.

The Preservation of Stored Blood with Sulphanilamide.

M. Novak (*The Journal of the American Medical Association*, December 16, 1939) states that complete bacteriostasis of the usual bacterial contaminants in blood stored for transfusion is effected by the addition of 20 milligrammes of sulphanilamide to each 100 cubic centimetres of blood. Blood so treated will not only fail to support bacterial growth for ten to fifteen days, but may actually become sterile in that time.

The Use of Heparin.

Roy D. McClure and Conrad R. Lam (*The Journal of the American Medical Association*, May 25, 1940) discuss their experiences in the administration of heparin and report the results of treatment in eleven cases; eight of the patients had post-operative pulmonary embolism, one had an embolus of the popliteal artery, another had thrombosis of the posterior tibial artery, and one had phlebitis. The authors describe the clinical course of each of their patients, illustrating the considerable variation in the amount of heparin necessary to elevate the clotting time to an arbitrary optimum level of fifteen minutes in different cases. The heparin was administered in 2% solution, except in cases in which indications to restrict fluids existed, in which event more concentrated solutions were used. The continuous intravenous drip method was preferred, and a vein in the leg proved more convenient for the administration than one in the arm. In most cases the authors inserted a medium-sized intravenous needle in a leg vein, where it was taped firmly in place, and after a day or two the patient was encouraged to move all extremities at will; but when the patients were uncooperative it was found essential to fasten a cannula in the vein by ligature. The authors consider that the administration of heparin may be discontinued after the patient has been ambulatory for two days, that the purified heparin available today is non-toxic when given intravenously, and that it is economically feasible to use it in treatment in selected cases.

Parenteral Sulphapyridine Therapy.

To determine any advantages that might accrue from the parenteral administration of sulpahpyridine, W. L. Whittemore *et alii* (*The Journal of the American Medical Association*, March 16, 1940) treated a series of 16 patients by the intravenous route and 13 by the rectal method; all were suffering from pneumococcic pneumonia. The initial intravenous dose consisted of two grammes of sodium sulphapyridine in 20 cubic centimetres of normal saline solution; this gave a blood level of 3·7 milligrammes within five to sixty minutes. In fifteen cases the dose was repeated in four to six hours; the average level in the blood was 6·3 milligrammes. A consistent response was obtained in 14 cases, as indicated by a drop to normal in temperature and pulse rate with a decrease in the toxic condition; six of these patients had uneventful recoveries. The remainder, however, experienced recrudescences of their fever from twelve to fourteen hours after their second injection; their condition was less toxic, and the blood level of sulphapyridine had dropped to an average of 2·2 milligrammes. Further treatment usually controlled these subsequent rises. The fact that many patients were found to maintain an adequate blood level for much longer than a twelve-hour period has so far made impossible any set routine method of administration beyond the first two doses. Four patients failed to respond to intravenous therapy and were found to be suffering from complications; the average total dose in this group was eight grammes, the smallest dose being two grammes and the largest 20 grammes. There was no vomiting, and nausea occurred in only one instance. Fourteen patients who did not appear too ill on admission to hospital had rectal treatment alone. Sulphapyridine was administered in doses of six grammes suspended in three ounces of water with from 0·66 to 1·0 gramme of sodium bicarbonate; this formed an effective non-irritating suspension of the drug and was introduced as a retention enema after a cleansing enema. At intervals of four hours doses of two grammes were employed, and later doses of three grammes. The blood levels were lower than those obtained by oral and intravenous therapy, averaging 3·0 milligrammes for the group. It was found that three times the oral dose was necessary to produce adequate blood levels. The clinical response was slower, but uniformly satisfactory. Only one patient exhibited nausea and vomiting, and there was no evidence of rectal irritability. This method of treatment is therefore useful for those patients who are not too seriously ill and who show gastric irritability. It is concluded that a desirable method of administering sulphapyridine to seriously ill patients is to give the sodium salt intravenously at first and follow this administration immediately by oral doses.

NEUROLOGY AND PSYCHIATRY.

Psychiatric Aspects of the Treatment of Cryptorchidism.

AFTER a detailed review of the ætiology and treatment of cryptorchidism both by surgery and by hormonic injection, Eugene Davidoff (*The Journal of Nervous and Mental Disease*, June, 1940) discusses the psychiatric aspects of the problem. He classifies cryptorchidism from the standpoint of behaviour as: (i) hypokinetic with (*a*) mental deficiency or (*b*) emotional sluggishness or both; (ii) hyperkinetic, (*a*) in patients of the anxious, unstable, neurotic type, showing masturbation and enuresis; (*b*) in nomadic children, truants, destructive and thieving types. The author believes that cryptorchid children presenting no behaviour problems are of the intellectually superior type. A specific cryptorchid personality cannot be said to exist. The behaviour patterns of cryptorchids vary with the underlying cause. Feelings of inferiority or psychological disturbances connected with undescended testicles are not common in the younger patients. Sluggish children with cryptorchidism are frequently masochistic, while in the hyperactive cases the children tend to be sadistic in their behaviour. Not all patients responded favourably to hormone therapy. The best response occurs among the younger group. But descent of the testicles does not always lead to improvement in the mental state. Cryptorchidism may be found entirely unassociated with any psychiatric entity. And in the final survey of the problem the author is inclined to place a restricted clinical value on endocrine therapy in this condition.

Artificial Fever Therapy in Multiple Sclerosis.

A. E. BENNETT AND MURRAY D. LEWIS (*The Journal of Nervous and Mental Disease*, August, 1940), in assessing the value of artificial fever therapy in multiple sclerosis, classify their cases into early, intermediate and advanced. In all there were 51 patients who had received at least four treatments by the Kettering hypertherm. The temperature was raised to 104° F. and maintained at that level for three or four hours. Forty of these patients were followed up over a period of four and a half years. In eight of the ten early cases a worth-while improvement was experienced and maintained; in four of these, it is claimed, a complete remission was achieved. In 13 of the 25 intermediate cases slight to pronounced improvement occurred, and 11 of the patients are still engaged in full- or part-time occupation. In the advanced cases and when the patient was bedridden fever therapy was found to be ineffective and possibly harmful.

Prolonged Coma after Insulin Hypoglycæmia.

DOUGLAS GOLDMAN (*The Journal of Nervous and Mental Disease*, August, 1940) describes the protracted coma of insulin hypoglycæmia as a very serious, frightening and potentially dangerous complication of the insulin treatment. He states that the condition is characterized clinically by a normal or elevated blood sugar level, continued stupor, hyperventilation, tetany and motor excitement and fever. Having noticed in one patient a transient bronzing of the skin after an extremely prolonged coma, he suggests an adrenal cortical deficiency as a cause of the condition; and he now treats this particular complication by the intravenous injection of large volumes of saline solution (1,200 cubic centimetres or more) and at the same time an intravenous injection of from three to ten cubic centimetres of adrenal cortical hormone ("Eschatin", Parke, Davis and Company). He believes that this régime constitutes the most effective means of combating prolonged coma, and he quotes cases in support of this contention.

Homosexuality Treated with "Metrazol".

WORKING on the hypothesis that sexual inversion is a symptom of underdeveloped schizophrenia, Newdigate M. Owensby (*The Journal of Nervous and Mental Disease*, July, 1940) presents six clinical histories of sexual inverts treated successfully by injections of "Metrazol" ("Cardiazol"). Five were male patients and one was a female; all exhibited overt homosexual trends. Treatment followed the orthodox lines for schizophrenia, and after a varying number of induced convulsions normal sexual desires became manifest. One male patient married four months after the completion of his treatment, and when interrogated ten months later stated that he had had no recurrence of his homosexual desires. The apparent success of this form of treatment led the writer to postulate the theory that the convulsion liberates the sexual libido from its previous fixation at the homosexual stage of the patient's psychosexual development.

"Metrazol" Reaction in Patients with Arterial Hypotension.

ALEXANDRA ADLER AND HOSEA W. MCADOO (*The American Journal of Psychiatry*, November, 1939) are of the opinion that arterial hypotension may be the cause of a somewhat alarming period of post-convulsive apnœa in patients receiving "Metrazol" ("Cardiazol") treatment. They cite two patients suffering from arterial hypotension, who, after the usual convulsion, became pulseless and lay motionless, as if dead, and whose breathing ceased for a period of from 19 to 25 seconds. Artificial respiration was applied and the pulse gradually returned, the carotid becoming palpable a few seconds before the radial. They believe this syndrome to be due to the poor vasomotor condition (the systolic pressure ranged from 68 to 100 millimetres of mercury), but consider it possible to carry the convulsion treatment to its conclusion.

Acute War Neuroses.

WILLIAM SARGANT AND ELIOT SLATER (*The Lancet*, July 6, 1940) distinguish between the neuroses which occur in soldiers under the trivial stresses incidental to army life without any of the severe strains imposed by actual fighting, and the acute neuroses seen in men who took part in the evacuation of Dunkirk by the British Expeditionary Force. These acute neuroses appeared in men of normal intelligence and personality who had a good civilian record, and they were directly concerned with an accumulation of great physical and mental strains—danger, anxiety, prolonged exertion, loss of sleep and great fatigue, intensified by irregular meals and perpetual bombardment, together with the sights of frightful destruction and death. The physical symptoms of profound exhaustion were apparent in many of these cases. The psychological symptoms belonged to mixed anxiety states and hysteria. The authors found that in the milder cases treatment by rest, aided by sedative drugs, free fluids and full diets was successful. Continuous narcosis was beneficial in the more severe cases. Hysterical symptoms, including amnesias, were relieved by hypnosis, produced directly or with the aid of barbiturates given intravenously. The prognosis in these acute cases has not yet been firmly established. Environmental stress has to be balanced against personality make-up; but a history of previous neurotic manifestation would generally serve to exclude the patient from front-line service.

Morgagni's Syndrome: A Clinical and Pathological Study.

MORGAGNI'S observations concerning hyperostosis of the flat bones of the skull and its association with mental changes and endocrine disturbances have been resuscitated by R. E. Hemphill and E. Stengel (*The Journal of Mental Science*, May, 1940), who describe in detail three fresh cases of this syndrome. The first patient was a young woman, presenting signs of organic dementia, who was found to have a diffuse hyperostosis of the vault of the skull; while in the second and third cases the hyperostosis was localized to the frontal and parietal bones and the mental disorder was of the paranoid type. Diffuse degenerative changes in the brain cortex were observed in the second case. Various pathological changes were found in the endocrine glands, especially in the pituitary. There was some atrophy of the thyreoid and cortical hyperplasia of the adrenals was present.

Prolonged Narcosis with Paraldehyde and "Dial".

NINETY psychotic patients were treated by M. B. Brody (*The Journal of Mental Science*, May, 1940) by prolonged narcosis induced by a combination of paraldehyde and "Dial". Two patients died. Vomiting was the most troublesome complication. Restlessness, pyrexia and albuminuria were also noted. Six patients had glycosuria. Twenty-five patients gained in weight; 42 lost weight and 13 showed no change. The technique is simple and the procedure is considered by the author to be reasonably safe, though not fool-proof. The results are similar to other types of continuous narcosis when used in the treatment of manic-depressive conditions. The author considers that the cost of the maximum daily dose of paraldehyde and "Dial" is less than one-third that of "Somnifaine"; and the somewhat unpleasant taste is the only disadvantage of the method.

Ascorbic Acid Levels in Patients Suffering from Psychoses of the Senium.

STIMULATED by the recent work of Plant, Altaman and Monouni, Douglas G. Remp, S. R. Rosen, John B. Ziegler and D. Ewen Cameron (*The Journal of Mental Science*, May, 1940) investigated the ascorbic acid levels in 15 patients suffering from senile psychoses and found them to be considerably lower than normal. They further found that these levels could not be raised by ordinary hospital diet containing 50 to 70 milligrammes of ascorbic acid per day. The addition of 300 milligrammes of ascorbic acid to the diet easily raised these levels, but no change was noted in the behaviour of the patients so treated. The authors suggest that there is a decreased capacity to assimilate ascorbic acid from the gastro-intestinal tract in aged psychotic patients.

Special Articles on Psychiatry in General Practice.

(Contributed by request.)

XVII.

CASE-TAKING AND ITS USE AS A REMEDIAL METHOD.

A WELL-KNOWN psychiatrist, the late Dr. Chisholm Ross, used to say that medicine was both an art and a science; in most cases the art was more important than the science. It can hardly be questioned that the dictum has a particular application to psychiatry. Its art lies largely in establishing and holding the confidence of the patient. The practice of the art commences with the first glimpse, the first handshake, the first conversation. Every manœuvre relating to contact with the patient has a bearing on treatment. Viewed in this light, the taking of the case history is not merely an excursion into the realms of diagnosis: it is also a vital part of treatment. Case taking is indeed a remedial method. Every detail is of great significance. The man in the street judges largely by first impression. The average patient uses a similar slide rule of values. It is essential, therefore, that the preliminary investigation must create this good impression.

Inherent Difficulties.

A psychiatric case history differs from an ordinary case history in that there are inherent difficulties. The first of these lies in the phenomenon of repression. Either consciously or unconsciously, the patient conceals the underlying factors of his illness. Some repressions are easily understood. He has a fear of suicide, of impending insanity or he fears ridicule. Self-esteem is a vital personality trait. He fears that the divulgence of his secret thoughts will render him an outcast from the herd of his associates.

At the onset the physician must give not merely an impression of sympathy and understanding, but must explain that the interview is secret and will not be divulged. Often it is an excellent gesture to take no notes. Occasionally it may be necessary to humour the patient by making certain that the door is closed and there are no listeners in the corridor. Many mental invalids are not merely suspicious, they are irritable to a marked degree and would try the patience of a Job. There is a further difficulty: our patients frequently not merely lack insight, they are incapable of powers of accurate description. The role of the psychiatrist is akin to that of the veterinary surgeon. He must learn to observe attitudes, the wrinkled forehead, the dejected appearance of the melancholic, the jaunty air of the manic, the other-worldliness of the schizophrenic. Such trivialities as clothing, hair cuts and finger nails and articulation may add a link to the chain of evidence.

Some Special Considerations.

A Word on Tact.

It is an established principle that a person's chief interest lies in himself. The actor and the psychiatrist have much in common. Both must divorce themselves from self in order to live the lives of others. They must have multiple personalities and be able at a moment's notice to translate themselves into another personality. A necessity for this type of mental gymnastics is very obvious in psychiatry. Only by entering into the spirit of another mind can its significance be appreciated.

A less obvious but equally important factor underlies the practice of tact. Tinker, tailor, soldier, sailor, richman, poorman, beggarman, thief, have their own idioms, idiosyncrasies and ideas. Only by appreciating their viewpoint and, so to speak, talking their language, is it possible to avoid infringing on their susceptibilities. Tact is required. It can be attained only by an ability to be all things to all men. For those who cherish their own individual foibles the prospect of selflessness may be irksome, if not impossible; but unless such self mastery can be obtained, then psychiatry is a closed door.

On Relatives and Friends.

The aim of the psychiatrist is to obtain a view of the whole life history of the patient. To this end the questioning of relatives and friends is an integral part of the case history. Often it is tedious and time-consuming. Two aspects are of special importance. One must be careful not to incriminate the relatives by relating remarks to the patient. The gleanings from the patient's own history must be divulged with caution to the relatives.

Most psychiatric literature gives the family history a high place in the prognosis assessment. Whilst this is undoubtedly true, it must be remembered that the patient's chief need is treatment. If the patient's own history reveals a morbid ancestry, he is disheartened at the outset. A better plan is to ignore the familial trends in all discussions with the patient. This can be obtained quite easily from the relatives, friends of acquaintances.

The Detection of Hallucinosis and Delusions.

The patient who possesses "insight" usually realizes that hallucinations and queer opinions are derided by other people. He may toy with them for months in solitude: often they are kept from his relatives and friends. The psychiatrist must pierce this barrier. There may be obvious clues, such as talking to oneself, laughing to oneself, covering the head with bedclothes *et cetera*. In other cases they must be angled for, as carefully as if a wary fish was being enticed. Leading questions, such as "You have noises in your head?" "They seem like dreams?" "They trouble you at night?" "You feel there is a conspiracy against you?" may be interspersed with reassuring remarks, as: "Of course we all hear such things when we are tired or upset." It is necessary to give the impression that such ideas are mere commonplace entities. If the patient is sensed as becoming hostile, the conversation may be turned into other channels. A repetition will be introduced at another time and from another angle. The efficiency of these simple measures is often surprising. The patient is anxious to unburden himself of his thoughts, and needs only a suitable stimulus in a congenial emotional atmosphere. It is, of course, essential that the interview be held without an audience.

On Sleep and Dreams.

No psychiatric interview is complete without attention to the question of sleep and dreams. If insomnia is present it is necessary to know whether the procuration or the prolongation of sleep be the main difficulties. Sometimes sleeplessness is due to specific fears, such as death during sleep or interference by others. The importance of dreams is obvious. Constantly recurring dreams often indicate the nature of an underlying psychic conflict.

Sexual Problems.

Whilst no hard and fast rules can be laid down concerning discussion of all sexual problems, there are two useful rules. Never introduce the sex topic until a measure of confidence has been attained. Never over-emphasize sex: it must be treated on matter of fact lines as just another of the instincts. Whilst no one will deny the importance of a balanced sexual life, undoubtedly much harm has been done by its over-emphasis. Almost every individual has had sexual traumata. It would be as logical to claim these as the causes of all mental invalidism as to claim a like relationship for bouts of constipation or indigestion.

The Physical Overhaul.

Every practitioner has his own plan for the physical overhaul. Preferably it is systematic. It must be thorough. The patient must feel that nothing has been missed. The physician must be satisfied that there is no physical basis for the nervous symptoms. At its conclusion the consultant should have a clear conception of nervous tone, as shown by the reflexes, and of the possibilities of endocrine imbalance.

On Test-Tube Diagnosis.

Chemical and mechanical diagnostic aids must be regarded as a mere extension of the physical overhaul. That they cannot always be completed at the first consultation is merely a matter of expediency and not of any innate difference. The physician should decide as soon as possible what investigations are necessary, and make arrangements accordingly. It is undoubtedly bad psychiatric practice to postpone from day to day such measures as X-ray examination, serological examinations, test meals, tests for allergy *et cetera*. Such a procedure produces doubt in the patient's mind. It is an implicit indication that the physician does not know his mind. Delay introduces the bugbear of psychiatric practice—the consideration of what will be the eventual cost. The routine tests—examination of the urine, hæmoglobin estimation, the performance of a Kline or Wassermann test—should be performed in every case as a part of the initial overhaul. The advantages of the routine performance of the Kline test are many. It is comparatively simple and therefore economical. The Kline test is remarkably accurate, and any positive results can be checked up by the Wassermann test.

This brief summary has been headed "Case Taking and its Use as a Remedial Method". The reasons are apparent. The first objective in the treatment of a psychiatric patient is that of transference. The patient must have an emotional relationship of faith in the doctor. A carefully planned and thorough examination will achieve this objective. It must be remembered that most psychiatric patients have passed through other hands. There is therefore a basis of comparison. If the physician fails to come up to the standards of his predecessors, the initial judgement is adverse.

The second great objective in treatment is to give the patient faith in himself. This can be obtained only by making certain of the part played by physical factors in the nervous disorder. If they are excluded, then the way is opened wide for the psychological approach. Undoubtedly this type of approach is both time and effort taking. It tries our patience and our endurance, but it produces results in therapy which will compensate for the labour involved. On the final analysis it is the only approach to the ideal of quick results.

John Bostock, M.B., B.S. (London), D.P.M., F.R.A.C.P.,
Research Professor of Medical Psychology, University of Queensland; Senior Psychiatrist, Brisbane General Hospital.

British Medical Association News.

SCIENTIFIC.

A meeting of the New South Wales Branch of the British Medical Association was held on May 23, 1940, at the Royal Prince Alfred Hospital. The meeting took the form of a number of clinical demonstrations by members of the honorary staff of the hospital. Part of this report appeared in the issue of October 19, 1940.

Cyst of the Third Ventricle.

Dr. Gilbert Phillips showed a male patient, aged forty-two years, who had been referred to him by Dr. Thomas, of Hurstville. He had had severe frontal headache for six months and had been subject to "dizzy turns" for six months. An alteration of temperament had occurred three months earlier. The patient had become noisy and resistive, and on February 13, 1940, was certified insane and admitted to Callan Park Mental Hospital. On April 2, 1940, bilateral papilloedema was noticed by Dr. Clifford Henry. There were no other objective signs.

On April 11, 1940, a ventriculographic examination disclosed a tumour protruding from the floor of the right lateral ventricle. On May 2, 1940, craniotomy was performed under local anæsthesia and the left frontal lobe was exposed. The ventricle was opened through a linear incision made in the middle frontal gyrus and a cystic tumour was disclosed presenting through the right foramen of Munro. The cyst was aspirated and gently freed from the edges of the foramen, a wide opening into the third ventricle being left. The patient was rational and conscious during the operation and subsequent convalescence was uneventful.

Oligodendroglioma.

Dr. Phillips next showed a female patient, aged thirty-five years, who had been referred by Dr. Cotter Harvey. She had suffered from headache for five weeks, from blurring of vision for one week and from loss of energy for one month. She had had fainting attacks for a period of four months and auditory hallucinations for one month; vomiting had been present for five weeks.

On April 8, 1940, 10 cubic centimetres of air were introduced into the ventricular system. The films revealed amputation of the anterior horn of the right lateral ventricle. On April 9, 1940, craniotomy was performed under local anæsthesia. A right frontal flap was reflected, and after the dura had been opened a brain needle was passed into the right frontal lobe and 20 cubic centimetres of yellow cystic fluid were aspirated. The operation was terminated at this point, and on the next day a second stage was performed; the whole right frontal lobe was excised, and at the same time a partly solid and partly cystic glioma was removed. The patient was rational and conscious throughout the operation, and the subsequent convalescence was uneventful except for some delay in healing at one corner of the scalp flap.

Glioblastoma Multiforme.

Dr. Phillips then showed a male patient, aged forty years, who had been referred by Dr. McGeorge. The patient had bumped his head on a boat three months earlier; he had suffered from headache and impaired memory for one month. Early morning vomiting and slurring of speech had been present for one month.

Lumbar puncture was performed; the cerebro-spinal fluid was under a pressure of 250 millimetres of water. On February 22, 1940, five cubic centimetres of air were introduced into the ventricle; the films revealed dislocation of the third ventricle to the right.

On February 29, 1940, craniotomy was performed under local anæsthesia. A left temporal flap was reflected and a large cyst, containing about 26 cubic centimetres of clear fluid, was removed from the temporal lobe. The patient had an uneventful convalescence and on March 19, 1940, was discharged from hospital, free from symptoms.

Headache recurred on April 30, 1940, and on May 1, 1940, a second craniotomy was performed under local anæsthesia through the original flap. A large solid tumour was now found occupying the situation of the previous cyst; it had apparently migrated from a deeper position following the operation for decompression. This tumour was entirely removed. After the operation the patient had a considerable degree of nominal aphasia and was discharged from hospital on May 28, 1940.

Left Cerebellar Cyst.

Dr. Phillips's fourth patient was a male, aged twenty-eight years; he had been referred by Dr. Greenaway. The patient had suffered from headache and nausea for two months and from hypersomnia for one month. Early morning vomiting had been present for six weeks, and early bilateral papilloedema was noticed. There were no other objective signs.

On February 14, 1940, a ventriculographic examination disclosed symmetrical internal hydrocephalus, indicating a lesion of the posterior fossa. On February 15, 1940, first-stage craniotomy was performed under local anæsthesia. The cerebellum was exposed and a cyst containing 26 cubic centimetres of fluid was aspirated in the left cerebellar hemisphere. On February 19, 1940, second-stage craniotomy was performed under local anæsthesia. A cerebellar cyst was completely removed. No histological evidence of new-growth was found.

Right Cerebellar Medulloblastoma.

Dr. Phillips next showed a female patient, aged four years, who had been referred by Dr. Norman Gregg. She had suffered from intermittent morning headache for twelve months; the headache was accompanied by vomiting, and the tonsils were suspected and removed. Six months prior to the meeting she commenced to walk to the right. In the last three months she had been using her left hand in preference to her right hand. Nystagmus was present on lateral deviation of the eyes; there were four diopters of papilloedema on both sides. Ataxia and hypotonia of the right extremities were present.

On March 28, 1940, craniotomy was performed under "Avertin" anæsthesia. The cerebellum was exposed and the right cerebellar hemisphere and a large intracerebellar glioma (medulloblastoma) were removed. At the time of the meeting the patient was quite well, had no headache and was able to walk about unaided.

Hour-Glass Fibroblastoma of the Spinal Cord.

Dr. Phillips's final patient was a female, aged thirty-nine years, who had been referred by Dr. Wilfred Evans. She had had girdle pain in the tenth and eleventh dorsal segments for two years. Unsteadiness, more pronounced in the right leg than in the left, had been present for four months. A painless blister had been present on the right heel for three months. Scalding water was spilt on the right foot and not felt six weeks prior to the meeting.

On examination thermanæsthesia was noted on the right leg. There was analgesia on the right leg, including the areas supplied by the eleventh and twelfth dorsal segments, and on the left thigh, including the areas supplied by the twelfth dorsal and the first and second lumbar segments. The sense of passive movement was lost in the right and left toes and ankles, and vibratory sense was lost in the right and left ankles, in the patella on each side, and in the iliac spines. The knee and ankle jerks were exaggerated. The abdominal reflexes were absent in the right lower quadrant.

On November 9, 1939, laminectomy was performed under "Avertin" anæsthesia. A large hour-glass tumour was exposed at the ninth spinal cord segment, firmly compressing the left side of the cord, a nodule of the tumour passing through the intervertebral foramen into the thorax. The

tumour was completely removed, together with its dural attachment.

The patient made a rapid recovery; she was walking about three and a half weeks after the operation, and at the time of the meeting was quite well at home, carrying out her customary domestic duties.

Cinematograph Film.

Dr. Phillips finally showed a cinematograph film illustrating the results obtained by section of the anterior funiculus of the spinal cord at the level of the second cervical vertebra. The patient was a girl, aged fifteen years, who exhibited continuous athetoid movements as the result of a cerebral injury at birth. After the operation all involuntary movements ceased and the patient was able to carry out voluntary movements, particularly of the lower extremities; this had previously been impossible, owing to the extensive spasticity. Dr. Phillips remarked that the interest of the case lay in the fact that a unilateral operation had produced cessation of involuntary movements on both sides; furthermore, it threw light on the situation of the supranuclear fibres in relation to the spinal sympathetic centres controlling the *dilator pupillæ*, as a Horner's syndrome developed on the same side as the operation. This result indicated that these fibres were placed in the anterior funiculus of the cord. No disturbance of respiration or micturition succeeded.

Hodgkin's Disease.

DR. A. T. NISBET showed a girl, aged seventeen years, whom he had first seen on January 31, 1935; at that time a swelling had been present for twelve months in the left side of the neck. This swelling gradually increased in size. A gland was removed and the pathologist reported the presence of Hodgkin's disease. Deep X-ray therapy was commenced on February 4; 350 *r* filtered through two millimetres of copper were given every day direct to the left cervical glands. A total dose of 1,400 *r* was administered, and treatment was complete on February 7, 1935. The same dose was repeated in September, 1936. In October, 1936, at the usual "follow-up" clinic, a hemispherical mass over the *manubrium sterni* and the right costal cartilages was discovered. This tumour was the size of half a golf ball. Further deep X-ray therapy was administered; 300 *r* filtered through two millimetres of copper were given to the *manubrium sterni*. The total dose at this time was 1,500 *r*. After treatment the mass subsided very rapidly and there had been no sign of recurrence either in that area or in the cervical glands.

In 1937 the patient returned to hospital with a large soft mass in the right side of the epigastrium; this time it was the size of a small orange. Further irradiation was given and this growth subsided; it could no longer be palpated.

Dr. Nisbet said that despite the numerous areas which over a period of five years had been invaded by Hodgkin's disease, there was no more clinical evidence of any infection. The patient looked well, had a good colour and appeared a normal healthy young woman.

Myeloid Leuchæmia.

Dr. Nisbet also showed a female patient, aged fifty-six years, suffering from myeloid leuchæmia. About six months prior to her first visit the patient had noticed that she was continually experiencing very large "bruises". She consulted a local doctor and medicine was prescribed. The bruises still persisted, and the patient was sent to hospital for further investigation.

On February 9, 1939, a blood count was made, with the following results. The erythrocytes numbered 3,920,000 per cubic millimetre, the hæmoglobin value was 85%, and the colour index was 1·0; the leucocytes numbered 150,800 per cubic millimetre, 38% being neutrophile cells, 26% myelocytes, 8% myeloblasts, 1% eosinophile myelocytes, 16% lymphocytes, and 8% monocytes; a few normoblasts were present.

Two doses of deep X-ray therapy were given, one to the anterior aspect and one to the posterior aspect of the thorax; 200 *r* were given in each case, treatment having been begun on February 15, 1939. Blood counts were made in the department of pathology at regular intervals, and the results were the following: on March 9, 1939, the leucocytes numbered 27,000 and the erythrocytes 4,430,000 per cubic millimetre; on April 20, 1939, the leucocytes numbered 9,125 and the erythrocytes 5,220,000 per cubic millimetre; on July 13, 1939, the leucocytes numbered 33,500 and the erythrocytes 5,050,000 per cubic millimetre; on September 7, 1939, the leucocytes numbered 56,000 and the erythrocytes 4,380,000 per cubic millimetre. At this stage further deep X-ray therapy was given, the dose being 300 *r* anteriorly and posteriorly to the thorax. Further blood counts gave the following results: on October 12, 1939, the leucocytes numbered 5,400 and the erythrocytes 4,620,000 per cubic millimetre; on November 23, 1939, the leucocytes numbered 3,950 and the erythrocytes 4,700,000 per cubic millimetre; on January 23, 1940, the leucocytes numbered 8,650 and the erythrocytes 4,900,000 per cubic millimetre; on March 21, 1940, the leucocytes numbered 16,750 and the erythrocytes 4,700,000 per cubic millimetre; on April 18, 1940, the leucocytes numbered 27,000 and the erythrocytes 4,650,000 per cubic millimetre; on May 16, 1940, the leucocytes numbered 46,500 and the erythrocytes 4,550,000 per cubic millimetre.

Dr. Nisbet said that deep X-ray therapy would again be given at the end of May. The case illustrated the small amount of irradiation necessary to keep the condition under control in some instances, and in addition it illustrated how, with small doses of X-rays, the number of erythrocytes would not only improve, but would remain within normal limits.

Osteolytic Sarcoma.

Dr. Nisbet's third patient was a female, aged thirty-eight years. The patient had had severe pain in the region of the left ilium and the sacrum, of twelve months' duration. The pain was first noticed after a strenuous game of tennis. The patient had previously consulted a doctor and had been given some "lamp" treatment, which did not improve the condition.

On examination an enlarged tumour the size of two fists was found arising from the posterior aspect of the sacrum, which was almost completely destroyed, except for a small fragment of the first sacral vertebra. An X-ray examination revealed a large soft-tissue mass in the pelvis and pronounced destruction of the left side of the sacrum; the only remaining portion was a small fragment of the first sacral vertebra. The condition was thought to be an osteolytic sarcoma.

Deep X-ray therapy was given between October 19 and October 31, 1939. A dose of 300 *r* daily, filtered through three millimetres of copper, was given to the posterior aspect of the pelvis; the total dose was 2,100 *r*. The patient reported again on January 16, 1940. A further X-ray examination was made; it revealed almost complete reduction of the soft tissue tumour in the pelvis and definite regeneration of bone in the sacrum. No further treatment was indicated. Four months later, on May 6, further X-ray films were taken; these revealed much apparent regeneration of bone in the sacrum, which was almost completely reformed. The soft-tissue tumour could not be distinguished. Dr. Nisbet pointed out that true osteolytic sarcomata were rare, but were usually very radio-sensitive, as had been shown in the case under discussion. Dr. Nisbet also showed a series of films demonstrating alteration in the lesion.

Thyreotoxicosis.

DR. HAROLD HAM showed a young married woman, aged twenty-four years, who had been presented at a previous clinical meeting. She had been referred to him suffering from severe thyreotoxicosis in January, 1938, by Dr. H. R. Poate. She had lost seventeen pounds in weight, and symmetrical enlargement of the thyreoid gland, mild exophthalmos and fine tremor were present. The basal metabolic rate was +75%.

Treatment consisted of three series of application of deep X-rays at monthly intervals. In each series three doses of 200 *r* were given in one week direct to the thyreoid gland. The kilovoltage was 210 and the filtration used was one millimetre of copper and one millimetre of aluminium.

Two months after treatment was started the basal metabolic rate was normal, and the patient had regained her normal weight. Since that time, over two years prior to the meeting, the patient had required no further X-ray therapy and no surgical or medical treatment. Her health at the time of the meeting was apparently normal, and even the exophthalmos had gone.

Dr. Ham said the case served to show what could be done with small doses of X rays in a severe case of thyreotoxicosis. He considered that X-ray therapy should be given a trial in the great majority of cases, especially in young subjects. The exceptions were cases in which the patient was in crisis or in which pressure symptoms were present. Small doses, such as had been used in the case under discussion, had no effect on the skin and did not produce adhesions, so that if subsequent operation was considered necessary, this was not made more difficult.

Carcinoma of the Mouth.

Dr. Ham also showed two patients suffering from carcinoma of the mouth, both of whom had been shown at a previous clinical meeting. One patient, a man, aged forty-nine years, had been referred to Dr. Ham in November, 1937, with a very extensive epithelioma; it involved the right lower alveolus from the mid-line in front to the

region of the third molar tooth behind, and extended onto the floor of the mouth and down into the right alveolo-labial sulcus. There was no obvious involvement of the cervical glands. The patient had first of all been given a short course of deep X-ray therapy to the region of the primary growth, and then radium was applied by means of a dental applicator, specially made to fit the patient. At the time of the meeting, two and a half years after his first treatment, the patient was in excellent health and showed no evidence of malignant disease in the oral cavity, where the mucosa looked normal, and no evidence of involvement of the cervical glands. He was being kept under regular observation.

The other patient, a woman, aged fifty-nine years, had been referred to Dr. Ham in August, 1938; she had an extensive epithelioma in practically the same situation as in the previous case, but in addition there were an indurated area in the floor of the mouth and a fixed gland mass in the submental region, 3·5 centimetres in diameter, with a discharging sinus in the centre.

Treatment consisted of deep X-ray therapy applied laterally to the right side of the jaw and to the submental region, fourteen treatments being given in all. No other treatment had been given, and the patient at the time of the meeting, twenty-one months after treatment, appeared well and showed no evidence of malignant disease.

Dr. Ham pointed out that this was an example of a squamous epithelioma, apparently typical in the histological picture; it was extremely radio-sensitive.

Carcinoma of the Fauces.

Dr. Ham also showed a woman, aged sixty-two years, who had been referred to him in February, 1938, suffering from an extensive carcinoma of the proliferative ulcerative type, occupying the left side of the fauces. It involved the whole of the anterior aspect of the pillar, a large part of the soft palate and the tonsillar fossa, and extended well down the lateral pharyngeal wall, the lower limit being difficult to determine on direct examination.

The patient looked cachectic, and biopsy was not considered justifiable. The lesion was considered too extensive for radium treatment, and deep X-ray therapy only was used. At the time of the meeting, over two years after treatment, the patient was well, with no evidence of malignant disease.

Dr. Ham emphasized that in each of these three cases the result had been achieved without any operative interference whatsoever.

Carcinoma Treated by Radium.

Dr. P. D. Braddon showed a large number of patients suffering from carcinoma in various regions treated by radium and radon (radium emanation). These lesions included carcinoma of the tongue, of the floor of the mouth, of the alveolus, of the fauces, of the inner canthus of the eye, of the dorsum of the hand *et cetera*, and illustrated results obtained by a variety of techniques with both radium and radon. Various moulds, for use at a distance, were also demonstrated, and also the use of the radon seed gun for radon gold seed implants.

A meeting of the Victorian Branch of the British Medical Association was held at the Mooroopna Base Hospital on June 8, 1940, Dr. H. C. Colville, the President, in the chair. The afternoon meeting took the form of a series of clinical demonstrations by members of the honorary medical staff of the hospital. In the evening Air-Commodore T. E. V. Hurley, C.M.G., Director of Medical Services of the Royal Australian Air Force, read a paper entitled "The Treatment of War Injuries" and afterwards answered a number of questions bearing on that subject.

Henoch's Purpura.

Dr. Herbert Smith showed a boy, aged ten years and four months, the youngest of four brothers in a healthy family. Without previous ill health a rash was found to be present when the lad wakened on March 18, 1940. At first the rash was purpuric, affecting the legs from the knees downwards; but it extended during the next few days up the backs of the legs and onto the buttocks. On March 22 he was admitted to the Tatura Bush Nursing Hospital in Dr. Smith's care, and on the following day he vomited and had a hæmorrhage from the bowels. The melena was sufficiently extensive to cause Dr. Smith to prepare to carry out a transfusion of blood, but that form of treatment was not adopted. During the succeeding three weeks the boy had several extensions of the trouble, losing a little blood from the bowel from time to time; his shoulders and wrists were mildly painful and transient swellings occurred, affecting at various times each of his hands, a shoulder, an eye and his feet, and when a swelling subsided a blood-spotted rash remained. Dr. Smith also described how the boy had complained repeatedly of spasmodic abdominal pain, at some times more severe than at others, and he mentioned the diverse nature of the skin lesions, some of which were purpuric, others macular, papular and erythematous, with urticaria. On April 17, after a consultation with Dr. Kennedy, of Shepparton, it had been decided to send the patient to Melbourne, and he had come into the care of Dr. Boyd Graham. As Dr. Boyd Graham was present at the meeting, Dr. Smith asked him to relate the further progress of the patient.

Dr. H. Boyd Graham said that the patient had been sent to him with a correct diagnosis and undergoing iron and calcium therapy. At that stage it did not seem possible to be sure that more serious hæmorrhages would not occur; but fortunately the progress had been very gratifying. On April 18 Dr. Reginald Webster carried out an examination of the blood; he had reported that the erythrocytes numbered 3,590,000 and the leucocytes 10,000 per cubic millimetre, the hæmoglobin value estimated by the Sahli method was 65%, the platelets numbered 288,000 per cubic millimetre, the coagulation time was four minutes and the bleeding time three minutes; the differential leucocyte count and the blood films revealed no abnormality. Dr. Graham went on to say that the purpura was not thromobcytopenic. The skin lesions resembled those of *erythema multiforme exudativum*; the boy had manifested angioneurotic œdema during the illness and on isolated occasions before it. The bleeding had rendered him moderately anæmic; he had shown no signs of blood in the urine or fæces, but he had continued to have abdominal discomfort of a less severe nature than before. The illness had run a mildly febrile course, and under treatment by rest in bed, by the administration of dicalcium phosphate powder, of vitamin *D*, of ferrous iron therapy and of local applications to the skin of *Linimentum Calaminæ Olcosum* (to which was added a little "Dettol"), the general condition of the boy had steadily improved. By April 24 the patient was comfortable, developing an appetite and recovering a healthy appearance; a week later he was allowed out of bed for a short time each day. Dr. Graham mentioned that at first there was a tendency to swelling of the feet, but that had passed away after the boy had been ambulatory for a few days, and it had not been associated with albuminuria. On May 7, 1940, the patient was sent home and again came under the care of Dr. Herbert Smith; but it could be seen by his healthy appearance at the time of the meeting that the improvement had been maintained. On June 2, 1940, Dr. Graham had received a note from the boy's mother conveying the information that the abdominal pain recurred less frequently and less severely and that fresh purpuric spots of an evanescent nature had been noticed.

Dr. Graham remarked that he had been particularly interested in the features of anaphylactoid purpura, of which the Henoch's purpura was only one of the incidents. He was at a loss to know what the allergen was, and had speculated that it might have been a hæmolytic streptococcus. He regretted that no investigation had been made of the ascorbic acid excreted in the urine or of the relationship, if any, of vitamin *C* deficiency to the condition. It was still rather early to be confident that no further developments would occur.

Dr. L. H. Hurley said that there was no doubt of the diagnosis. He believed it was true to say of Henoch's purpura that they did not know the cause, but that there were two theories, the infective and the anaphylactoid. Among practical points of interest Dr. Hurley mentioned that there was rarely a true purpura, but practically always an inflammatory reaction manifested by erythematous and raised lesions. There was a liability to lesions elsewhere than in the bowel and in the skin—for example, involvement of the joints or of the kidneys. Not only were there evidences of hæmorrhage in the urine, but there might be manifestations of true nephritis with, as Osler had pointed out, a tendency to progress to chronic nephritis. Dr. Hurley mentioned the amount of hæmorrhage from the bowel in the case under discussion as an unusual feature; it was rarely so bad that transfusion had to be considered. With reference to treatment, Dr. Hurley added that all that could be done was to treat the symptoms as they appeared.

Dr. M. D. Silberberg raised the question whether deficiency of ascorbic acid was a factor in the ætiology and whether treatment with large dosage of ascorbic acid would be likely to be of benefit.

Symptomless Swelling in the Neck.

Dr. Stuart Thomson, on behalf of Dr. W. L. Armstrong, showed a married woman, aged thirty-two years, with a symptomless swelling in the neck. In 1930 her appendix had been removed and in 1933 cholecystectomy had been per-

formed, but in other respects her health was good. She had consulted Dr. Armstrong on account of fullness in the left side of the neck, and he had felt a lump there; but it had caused no alteration of the voice or discomfort on swallowing, although in the skiagrams it would appear that the swelling extended well down behind the first rib. It was not possible to delimit its lower extent by palpation. In an attempt to investigate the nature of the swelling further skiagrams had been prepared with the œsophagus filled with a radio-opaque substance. From the skiagrams Dr. Thomson showed that there was a distortion to the right in the course of the œsophagus and that the aortic "knob" was unduly prominent and contiguous with a double-outlined shadow above and to the left of the heart shadow extending up into the neck. Dr. Thomson added that the patient's serum had failed to yield the Wassermann reaction and that that day she had mentioned to him that for the past two weeks she had had a feeling that something was crawling inside her ear.

DR. M. D. SILBERBERG said that he would have the temerity to open the discussion by expressing the opinion that the tumour was not of thyreoid origin. He had formed the suspicion that it might be a superior mediastinal tumour with malignant tendencies. It was a double swelling and the outer part was glandular. An important point against the view he had expressed was the fact that the woman was in very good health. Malignant mediastinal tumours caused interesting syndromes. He remembered one which produced definite swelling in the neck and sufficient pressure on the veins to increase the size of the collar from 15 to 17 inches, though the patient had lost considerable weight. In another instance there had been sufficient flattening of the aorta to raise the question of aneurysm; but the patient was not syphilitic. The condition was associated with a rapidly developing symmetrical swelling in the neck.

DR. G. A. PENINGTON said that the outline of the œsophagus contained only the normal indentation and that there was no suggestion of a neoplastic process at work. He was not even satisfied that the aortic knuckle was enlarged, and thought that it would be worth while to investigate the cervical portion of the spine radiographically and also to perform Casoni, intradermal and hydatid complement fixation tests, because he considered that the tumour had the firm elastic feel of a confined hydatid cyst.

AIR-COMMODORE T. E. V. HURLEY thought that the swelling was probably of thyreoid origin with retrosternal enlargement. He agreed with Dr. Penington that the œsophageal distortion had nothing to do with it. The swelling was rather far from the mid-line and did not move with deglutition: but an adenoma might be present in relation to a tongue of normal thyreoid tissue.

DR. A. E. COATES said that from a consideration of the anatomical structures the swelling could arise from the thyreoid gland or from lymphatic glands, and that from the pathological point of view it was likely to be caused by hæmorrhage into an adenoma of the thyreoid gland. That swelling might be quite large and fixed, although the state of health of the patient appeared to be good; if the condition were malignant, on the other hand, he would expect the swelling to be harder and the patient would not be in such good health. He said he did not think the swelling felt at all like a hydatid cyst.

DR. PAUL JONES said that he thought that the lump was in the posterior part of the thyreoid gland, well behind the sternomastoid muscle, in a position where the thyreoid normally was found. The swelling had been there for six months and the patient had continued to be very well. He thought the radiographic appearances were those of the ordinary amount of aortic compression associated with the filling of the œsophagus with radio-opaque material.

DR. C. J. O. BROWN raised the question of aberrant thyreoid tissue which sometimes occurred along the sternomastoid muscle lateral to and separate from the thyreoid gland itself. He said that the aberrant bodies were really glandular metastases from a tumour of the thyreoid reproducing the structure of the original gland. He had seen a case in which five aberrant lumps, removed and examined microscopically, were found to have a lymph gland structure filled with cells which were obviously thyreoid cells exactly similar to the original adenoma. The patient went to the country, and six weeks later it was found that a gland mass had recurred which, when dissected out, was found to be similar to the previous ones. He added that, so far as he knew, the patient had remained perfectly well during the four years which had elapsed since these events.

As a suggestion for treatment, Dr. Brown thought that the mass in the neck should be exposed with the object of surgical removal; he thought that there was no abnormality in the mediastinum apart perhaps from some thickening of the pleura.

DR. ANNIE L. BENNETT said that in interpreting the skiagrams she had regarded the appearances of the filled œsophagus as normal, but thought that the shadow above the aortic knuckle was of pathological import; if a hydatid cyst was present she would have expected it to show more distinctly in the structures of the neck.

Dr. Thomson, in reply, said that the swelling had been regarded as an adenoma of the thyreoid gland with adhesions to the surrounding fasciæ; it was placed deeply in the neck, and he thought it went down into the chest, as he could not get his finger between it and the clavicle.

(To be continued.)

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 210, of October 10, 1940.

AUSTRALIAN MILITARY FORCES.

Army Headquarters.

Lieutenant-Colonel J. H. Anderson, C.M.G., C.B.E., Unattached List (A.A.M.C.), is appointed Assistant Director-General of Medical Services, and to be stationed at the office of the Military Liaison Officer, London, 19th August, 1940.

Australian Army Medical Corps (Permanent).

To be Major (temporarily).—Captain W. V. Russell, 10th July, 1940.

NORTHERN COMMAND.

First Military District.

Australian Army Medical Corps.

To be Captain (provisionally)—Albert Stephen Furness, 22nd August, 1940.

Australian Army Medical Corps Reserve.

To be Honorary Captains—David Aubrey Arnot Davis, Victor Plant Webb and William Blackburn, 21st August, 1940.

EASTERN COMMAND.

Australian Army Medical Corps.

To be Captains (provisionally)—Angus Johnston Murray, Kenneth Beeson Noad, Louis Samuel Loewenthal, Alfred Charles Thomas, Walter Gerald Holt, Arthur Bernard Sullivan, Innes Albert Brodziak, Charles Ruthven Bickerton Blackburn, Reginald Henshall Bettington, John Howell Halliday, Edgar Frederick Thomson, Clifford Stirling Colvin and Eric Hyman Goulston, 21st May, 1940; Norman Henry Rose, Norman Richard Wyndham and Arthur Liddon Webb, 24th May, 1940; John William McNamara and Maurice Philip Susman, 20th June, 1940.

SOUTHERN COMMAND.

Third Military District.

Unattached List.

Lieutenant-Colonel J. H. Anderson, C.M.G., C.B.E., is appointed from the Reserve of Officers (A.A.M.C.), 18th August, 1940.

WESTERN COMMAND.

Australian Army Medical Corps.

Major E. J. T. Thompson, M.C., is appointed to command 13th Field Ambulance, and to be Lieutenant-Colonel (temporarily), 1st June, 1940, *vice* Lieutenant-Colonel L. E. Le Souef, seconded to A.I.F.

MEDICAL OFFICERS FOR THE NINTH DIVISION, AUSTRALIAN IMPERIAL FORCE.

THE Director-General of Medical Services announces that in connexion with the formation of a ninth division, Australian Imperial Force, additional medical officers for the following units will be appointed:

Two field ambulances	18
One casualty clearing station	8
One general hospital	19
Six regimental units	6
One field hygiene section	1
Total	52

No allotment of appointments to these positions will be made to individual States for the medical officers. The rank and file personnel, however, for each unit will be raised as far as possible from the States concerned.

In addition, 20 medical officers will be required to complete establishments for units already overseas.

Correspondence.

THE USE OF HISTAMINE IN THE TREATMENT OF NEURO-VASCULAR HEADACHE.

Sir: Referring to a report by W. Lister Reid, on "The Use of Histamine in the Treatment of Neuro-Vascular Headache", published in The Medical Journal of Australia on October 5, 1940, it is surprising to note an entire absence of any mention of the part played by allergy in the production of headache, not only typical migraine, but also similar conditions, such as described by Reid.

Within recent years the experience of a number of workers in allergy has been published, showing that 50% or more of such cases can be relieved of symptoms by dietary management following investigation regarding offending foods and sometimes by inoculation following the discovery of inhalant allergens. My own experience has convinced me that the facts have not been overstated, as about 70% of my cases have proved to be allergic and have been either completely or partially relieved of their symptoms. It is surprising that Reid has either overlooked all references in the literature to such work or chosen to ignore them, and it would be most unfortunate for patients if they should be subjected to scores of histamine injections without first being given the benefit of investigation concerning possible allergic factors. Perhaps it is advisable to add that these investigations do not merely consist in a skin test, and should be undertaken by an expert, otherwise negative results mean nothing. Some success has attended inoculation of histamine in allergic disorders, and even the prolonged and intensive use of this method appears worth while in severe cases of headache after the elimination of various possible ætiological factors has failed to give relief. Treatment with histamine was suggested by Dale's experimental work, which indicated the liberation in the tissues of H-substance in the allergic or anaphylactic reaction. This gave hope that if by inoculation of gradually increasing doses of histamine a tolerance to the poison could be produced, the patient would become free from symptoms of allergic reaction whenever this took place. So far the results have been disappointing in comparison with those achieved by elimination *plus* desensitization; but Reid's results suggest a useful application of the method providing the cases are carefully selected.

Yours, etc.,

D. L. Barlow,

Shell House,
170, North Terrace,
Adelaide.

October 12, 1940.

SELF-TREATMENT, OR A PATIENT WHO TELLS.

Sir: On September 8, 1940, I was called to see a patient, G.A.L., aged thirty-six years, who has since written out his history prior to sending for me. He heads it: "Self-treatment, or a patient who tells".

> Friday: Sore throat and bad cold. Treatment (self): During day, two A.P.C. powders, two or three potassium chlorate tablets; 5.30 to 6 p.m.: six rums and ginger ale; 7 p.m.: large hot roast dinner; 8.30 p.m.: fall asleep in chair and wake up at about 9.30 p.m. with the shudders; 9.30 p.m.: mix three "Aspros" by mistake with lemon juice instead of water and gargle with same and take three "Aspros" internally and wash down with hot rum, lemon and sugar. Go to bed; 12 p.m. [*sic*]: vomit on large scale, also on carpet.
>
> Saturday: 7.30 a.m.: Had large dose of "Hardy's Stomach Remedy"; able to walk around, but had severe aching pains in legs and back. Also had a very livery feeling and eyes did not seem to focus too well. Decided this day to concentrate on "De Witt's Kidney Pills" (they must be good because the advertisement says so, and also green's my favourite colour) and took three pills during the day and two at night. Severe dysentery all day.
>
> Sunday: Stayed in bed all day. Pains all over stomach and in front of body. Took another dose of "Hardy's". Back cured by "De Witt's" (there's truth in advertising!). Had glass of warm milk and nutmeg during day to prevent me from falling to pieces. 7 p.m.: Asked Dr. B. to call for a little chat.

This screed omits the fact that the patient also took four "liver pills" on Sunday morning.

However, when first seen, he looked like a person with a typical influenza. His face was flushed, eyes red, cough and sore throat marked, temperature 101·4° F. His chest was musical and his abdomen slightly tender all over. He was given a mixture for the influenza and some bismuth and belladonna for what was considered to be intestinal colic, as much from self-medication as otherwise. He was asked to let me know if there was no improvement next day, but it was not until the following day that he sent for me again. This time, although the cough was still there, a brief examination revealed marked tenderness in the right iliac fossa. Removed to hospital, a spinal anæsthesia was decided upon on account of the influenzal condition. As soon as the abdominal muscles relaxed a mass could be seen. On opening into the peritoneal cavity this was seen to be caused by heaped-up omentum. This was cautiously dissected away and revealed a large gangrenous appendix coming from a phlegmonous *caput caecum coli*. It was finally delivered and removed, though it was impossible to invaginate the stump, which was sterilized. The abdomen was closed without drainage. Recovery was uneventful, except for some fat necrosis.

I send this history along for any interest it may have if you consider it worth publishing. One sees so many cases of "gastric 'flu"!

Yours, etc.,

A. Bulteau.

7, Pittwater Road,
Gladesville,
New South Wales.

October 13, 1940.

THE AFTERMATH OF WAR AND RECONSTRUCTION.

Sir: That a new world order will follow the ruin and destruction inflicted by the present war seems evident, but that it will be a desirable world order is by no means so plain.

The fruits of the last war were a steady drift to dictatorship, overt in totalitarian countries, hidden in democratic countries (though no less real—think of our numerous dictatorial boards and of the *National Security Act*!), and a new war. Unless democrats think and act, the whole world will become totalitarian whoever be victor in the war. War gives us martial law; martial law is dictatorship; law becomes custom and we learn to think in dictatorial terms; we are perverted in our inmost being. Australians rejected the national insurance plan and the marketing referendum, knowing that both threatened their liberty, but they have accepted the *National Security Act* because of the war. One of our after-war problems will be to get rid of it!

As you said in your editorial of September 21 last, virtue, love and idealism are the only regenerators of a lost humanity, and a Christian morality must be practised in private life, in industry, and in the public life of the State. I believe that most Australians desire this, but that they have no idea of how to achieve it. Motives and ideals are not enough (though the necessary foundation), ways of carrying them out must be found. We can only save ourselves (and the world with us) by taking thought and by demanding a public inquiry into the problems of the day, and especially the monetary problems of the day. In Mildura a group of 31 leading men is organizing a demand for such an inquiry, while in other places small groups of women are studying the social problems which will face us after the war. Not being in imminent danger of our homes falling about our ears, Australians have sufficient serenity to deal with these problems now. Let us do so, otherwise when the war ends no one will know what to do, and we will start on the inevitable journey towards a new war, just as we did last time!

In the present state of the world, indeed throughout history, totalitarian countries purchase economic security at the price of freedom and of war, while democratic countries buy freedom at the price of economic security (unemployment, wage slavery, tenancy) and of war. All desire freedom and security—none gets both; all get war! Why is this so?

Scriptural history is clear on the subject. The prophets had no hesitation in teaching that war was the result of the disobedience of the laws of Moses—that it was the fruit of the exploitation of one by another, and especially of the practice of usury. Now our civilization is built on legalized usury! There is a direct conflict between the teachings of

our religion and our practice. "Religion is religion, business is business!" No wonder that moral scepticism prevails!

Usury is the inevitable consequence of using a commodity-money (barter, gold standard, market-basket of commodities, price index). A commodity-money entails debt and usury (politely called interest) and entirely neglects the human being on whose life and work the existence of a nation depends. Money should be attached to the human being (of whatever age, sex or occupation) instead of to the thing he has made. Such a money (Wice currency), based on labour (work-time) instead of goods, has been devised.

If we exchange our present tool of exchange for a better one, one which recognizes the existence of every human being from birth to death, we will abolish debt, usury, unemployment, malnutrition, and thus be able to practise what we believe, to love our neighbour as ourselves, and to solve our many problems. We will achieve freedom and security for all.

May your readers join in the demand for an inquiry!

Yours, etc.,

MARY C. DE GARIS.

Geelong,
October 14, 1940.

Obituary.

THOMAS JAMES HENRY.

WE regret to announce the death of Dr. Thomas James Henry, which occurred on October 17, 1940, at Manly, New South Wales.

Notice.

THE next clinico-pathological conference arranged by the Post-Graduate Directors of Medicine, Surgery and Pathology will be held at the Prince Henry Hospital, Little Bay, on Monday, October 28, 1940, at 4.30 p.m. The subjects will be: (i) cases for diagnosis and discussion, (*a*) acute conditions of the abdomen, (*b*) blood dyscrasia; (ii) post-mortem demonstration of lesions in leprosy. A cordial invitation to be present is extended to all medical practitioners.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Burfitt, Thomas Owen, M.B., B.S., 1938 (Univ. Sydney), 110, Elizabeth Bay Road, Elizabeth Bay.

Books Received.

"J. F. Sutherland's First Aid to the Injured and Sick", revised and rewritten by H. Sutherland, M.D.; Forty-second Edition; 1940. Edinburgh: E. and S. Livingstone. Demy 32mo, pp. 76, with illustrations. Price: 6d. net.

"Encyclopædia of First Aid", by M. J. Hogan; 1940. Sydney: M. J. Hogan; Gordon and Gotch Limited. Crown 8vo, pp. 122. Price: 2s. 6d. net.

"Elementary Atlas of Histology", by Burton Bradley, M.B., Ch.M., M.R.C.S., L.R.C.P., D.P.H., with a foreword by J. B. Cleland, M.D.; 1940. Australia: Angus and Robertson Limited. Crown 4to, pp. 122. Price: 15s. net.

"Starost", issued by the Institute of Experimental Biology and Pathology; 1940. Kiev: Ukrainian Society for Cultural Relations with Foreign Countries. Super royal 8vo, pp. 490, with illustrations.

"The Periodicity and Cause of Cancer, Leukæmia and Allied Tumours, with Chapters on their Treatment", by J. H. D. Webster, M.D., F.R.C.P.E., F.F.R.; 1940. London: Baillière, Tindall and Cox. Crown 4to, pp. 193, with illustrations. Price: 12s. 6d. net.

"The Anatomy of the Eye and Orbit, including the Central Connections, Development and Comparative Anatomy of the Visual Apparatus", by E. Wolff, M.B., B.S., F.R.C.S.; Second Edition; 1940. London: H. K. Lewis and Company Limited. Crown 4to, pp. 384, with 242 illustrations. Price: 31s. 6d. net.

"Organization, Strategy and Tactics of the Army Medical Services in War", by T. B. Nicholls, M.B., Ch.B., with chapters by A. S. Glynn, M.B., Ch.B., K.H.S., R.A.F., A. R. Laurie, M.B., Ch.B., D.M.R.E. (T.A.), and F. G. Lescher, M.C., M.A., M.R.C.P. (T.A.); Second Edition; 1940. London: Baillière, Tindall and Cox. Royal 8vo, pp. 504. Price: 15s. net.

"A Method of Anatomy, Descriptive and Deductive", by J. C. B. Grant, M.C., M.B., Ch.B., F.R.C.S.; Second Edition; 1940. London: Baillière, Tindall and Cox. Crown 4to, pp. 816, with 651 illustrations. Price: 33s. net.

Diary for the Month.

OCT. 31.—New South Wales Branch, B.M.A.: Branch.
NOV. 1.—Queensland Branch, B.M.A.: Branch.
NOV. 5.—New South Wales Branch, B.M.A.: Organization and Science Committee.
NOV. 6.—Western Australian Branch, B.M.A.: Council.
NOV. 6.—Victorian Branch, B.M.A.: Branch.
NOV. 7.—South Australian Branch, B.M.A.: Council.
NOV. 8.—Queensland Branch, B.M.A.: Council.
NOV. 12.—Tasmanian Branch, B.M.A.: Branch.
NOV. 12.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
NOV. 19.—New South Wales Branch, B.M.A.: Ethics Committee.
NOV. 20.—Western Australian Branch, B.M.A.: Branch.
NOV. 21.—New South Wales Branch, B.M.A.: Clinical Meeting.
NOV. 22.—Queensland Branch, B.M.A.: Council.
NOV. 26.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

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